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SURGERY

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SURGERY

VOL. 27 APRIL, 1950 NO. 4

Original Communications

ANORECTAL ANOMALIES

A STATISTICAL STUDY OF ONE HUNDRED SIXTY-FIVE CASES WITH SPECIAL REFERENCE TO "DISTAL-LOOP TROUBLE"

CHARLES W. MAYO, M.D.,* AND ROBERTA G. RICE, M.D.,† ROCHESTER, MINN.

THE first reported successful treatment of a patient with imperforate anus is accredited to Paulus of Aegina in the seventh century. He passed a bistoury through the perineum, and later dilated the opening with bougies. In the United States the first successful operation for this condition was reported in 1790 by Campbell.[1]

Rhodes[2] stated that congenital anomalies of the anus and rectum occur about once in every 5,000 babies born. In this country, where there are more than 2,500,000 babies born each year, one would then expect to find about 500 children born each year with this condition.

In the years 1910 through 1947, 165 patients who had an anorectal anomaly were registered at the Mayo Clinic.

A brief résumé of the embryology of the anorectal region helps in the understanding of the pathogenesis of these abnormalities. In the 3-week-old embryo, the urinary tract (allantois) and the lower part of the intestine (hind-gut) are one cavity, the cloaca. The cloaca comes from the epiblast (ectodermal) lying in front of the spinal column. This cavity becomes divided into anterior and posterior portions by the urogenital membrane. The anterior chamber becomes the urinary bladder and the genitals. The posterior chamber forms the primitive rectum, which is also called the mesenteron or postallantoic gut. The primitive rectum descends toward the perineum where, about the seventh week of gestation, it meets an infolding of epiblast (ectodermal) called the proctodeum which becomes the anus. The union of the primitive rectum and the proctodeum is at the mucocutaneous line. Malformations in this region are due to failure of the urogenital membrane to separate the rectum completely from the bladder. This failure causes abnormal communications between the bowel, bladder, urethra, and vagina. Second, malformations in this region are due to failure of the proctodeum to meet and unite with the primitive rectum, causing imperforate rectum, or congenital stricture. Drueck[3] stated that in females the lower level of the rectum is usually about 2 cm. from the perineum, and in males about 3 cm. For a more detailed presentation of the embryology of this condition one is referred to the articles by Ladd and Gross,[4, 5] Lee,[6] Pennington,[7] and Wilson.[8]

Since Ladd and Gross published their comprehensive study of anorectal anomalies,[5] the method of classification which they proposed has been widely accepted. Crowell and Dulin,[9] Dmytryk,[10] and Lee[6] have used Ladd and

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Gross's method in their studies of anorectal anomalies. The chief advantage of this type of classification is its use in determining the necessary form of treatment, and in predicting the probable results of treatment in any given patient. So far as possible we tried to adhere to their classification. Hence, we classified as type I anomaly the malformation of a patent anus and rectum, but with a stenosis either of the anus or of the rectum. Type II anomaly included all conditions in which there was an imperforate anus and the obstruction was membranous. In type III malformation the anus was imperforate and the rectal pouch ended blindly some distance above the anus. In the type IV group the anus and sphincter and the lower portion of the rectum were all normal, but the upper portion of the rectum ended blindly and was separated by a variable distance from the lower pouch. Because some of the patients had had their primary treatment more than thirty years before, and that elsewhere, it was not always possible to be sure whether the patient belonged in type II or type III. This was especially true in female patients with rectovaginal fistulas.

The incidence of anorectal anomaly by type and sex is summarized in Table I. In our series of 165 cases there were 85 males and 80 females, an incidence of 51.5 per cent and 48.5 per cent, respectively. Other authors[11] also have found the condition to occur about equally in the two sexes. About 91 per cent of the males and 98 per cent of the females were of types II and III.

TABLE I. INCIDENCE OF ANORECTAL ANOMALY BY TYPE AND SEX

TYPE	TOTAL		MALE		FEMALE	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
I	4	2.4	3	3.5	1	1.2
II	62	37.6	22	25.9	40	50.0
III	95	57.6	56	65.9	39	48.8
IV	4	2.4	4	4.7	0	0
Total	165	100.0	85	100.0	80	100.0
Per cent total	100		51.5		48.5	

Stieda[12] classified anorectal abnormalities as with or without fistulous communication of the terminal portion of the bowel. In his group, 54.3 per cent had fistulas. Tables II and III summarize the incidence and site of the fistulas found in our 165 cases. Of the males 70.6 per cent and of the females, 95 per cent, or 82.4 per cent of the 165 patients, had a rectal fistula. In 56 of the 60 male patients having rectal fistulas the site was between the rectum and the genitourinary tract. In 12 of the males the actual site of the fistula was not visualized. Most of these 12 were newborn infants who passed meconium through the penis. Five of the females had fistulas between the rectum and the urinary tract. Four of these 5 had no vagina and 1 had rudimentary double vaginas.

The diagnosis of imperforate anus is usually made by the nurse, who tries to take the patient's temperature by rectum, or who notes meconium coming with the urine. Keiller[13] in 1924 was the first to use a barium suspension injected into the distal colonic stoma to demonstrate the site of obstruction of the

TABLE II. INCIDENCE OF FISTULA BY TYPE AND SEX

	TOTAL			MALE			FEMALE		
		FISTULA			FISTULA			FISTULA	
TYPE	CASES	NUMBER	PER CENT	CASES	NUMBER	PER CENT	CASES	NUMBER	PER CENT
I	4	2	50.0	3	2	66.7	1	0	0
II	62	53	85.5	22	14	63.6	40	39	97.5
III	95	77	81.1	56	40	71.4	39	37	94.9
IV	4	4	100.0	4	4	100.0	0	0	0
Total	165	136	82.4	85	60	70.6	80	76	95.0

lower loop. This procedure is likely to lead to further difficulty for the patient because of the barium residue left in the blind distal loop. This difficulty occurred in 3 of our cases. Wangensteen and Rice[14] in 1930 made an important contribution to the diagnosis of the site of the rectal obstruction by advocating the taking of roentgenograms of the infant's abodmen with the child held in an inverted position so as to let the air in the intestine rise to the site of the obstruction. Wilson[8] has expressed the belief that one can get a more accurate picture of the terminal portion of the bowel at its lowest point by using repeated pictures taken with the baby lying on his side with the knees firmly flexed against the abdomen. In making the picture he has the roentgenologist push his finger into the child's perineum at the normal anal site.

Eighteen of the 165 patients were seen within the first forty-eight hours of life. Forty-eight were seen for the first time from 2 through 12 months of age. Sixty-eight were from 2 through 11 years of age, and 19 were more than 12 years old when they were first registered.

TABLE III. SITE AND SEX DISTRIBUTION OF FISTULAS PRESENT

SITE	MALE	FEMALE
Between rectum and urinary tract	56	5*
Rectovesical fistula	17	2
Rectourethral fistula	27	1
Rectocloacal fistula	0	2
Site not localized, probably rectourethral	12	0
Rectovaginal fistula	0	61
Rectoperineal fistula	4	10
Total	60	76

*Four had no vagina, and one had rudimentary double vaginas.

Seventy-three (44 per cent) of the 165 patients had some congenital anomaly other than the anorectal malformation. Tables IV and V summarize the incidence and type of associated congenital anomaly found. Of the males 51.8 per cent and of the females 36.3 per cent were found to have some associated anomaly. In 26 of the 44 males having associated congenital deformities, the anomaly was of the genitourinary tract. Four of the 15 deaths in this series were directly due to the associated congenital anomaly. Three of the patients who died had tracheoesophageal fistulas, and 1 had severe congenital heart disease. Ashley[15] in 1941 stated that about 30 per cent of patients with tracheoesophageal fistula have associated anorectal anomalies.

TABLE IV. INCIDENCE OF ASSOCIATED CONGENITAL ANOMALY

SEX	TOTAL CASES	ASSOCIATED CONGENITAL ANOMALY	
		NUMBER	PER CENT
M	85	44	51.8
F	80	29	36.3
Total	165	73	44.2

The method of treatment of anorectal anomalies was dependent on the type of the anomaly and the age of the patient. If there was only a thin membrane between the proctodeum and the rectum the procedure of choice was to cut or puncture the membrane and observe the patient carefully, using repeated dilatations to avoid rectal or anal strictures. When the anus was absent but a depression or dimple was present, when one could demonstrate the presence of rectal sphincters, and also, when bulging of the blind end of the rectum could be seen, the usual treatment was a proctoplasty bringing the rectal mucosal edges to the anal skin margin. When the rectum was high, one either performed colostomy immediately or attempted a perineal exploration. Usually in such cases a fibrous cord was found between the end of the rectum and the site of the anus. By following this, one could find the rectal mucosa, free it, and bring it down to the edges of the anal skin. However, in 12 (12.6 per cent) of the 95 cases of type III imperforate anus, the perineal exploration was unsuccessful. The blind end of the rectosigmoid could not be found. We believe that in the newborn male infant with a high rectum the perineal exploration should be postponed. This is especially true when there is evidence of rectovesical or rectourethral fistulas. In these patients colostomy should be performed as soon as possible and care should be used to separate the proximal from the distal barrel of the stoma. In the newborn female infant with a rectovaginal fistula, repeated dilatations of the fistula usually sufficed until the child was old enough, and the tissues were well defined enough, to allow a successful rectovaginal plastic procedure. The latter is recommended because of the relatively high

TABLE V. TYPE OF ASSOCIATED CONGENITAL ANOMALY PRESENT

TYPE	TOTAL*	MALE	FEMALE
Genitourinary	36	26	10
Horseshoe kidney	2	2	0
Absent vagina	4	0	4
Double vagina	2	0	2
Umbilical hernia	14	5	9
Skeletal anomaly	16	9	7
Congenital heart disease	13	7	6
Inguinal hernia	4	3	1
Tracheoesophageal fistula	3	2	1
Cleft palate	2	1	1
Infantilism	1	0	1
Hemangioma	1	0	1
Deformed ear	1	1	0
Hemophilia	1	1	0
Atelectasis right lung	1	1	0
Cystic hygroma	1	1	0

*Since a patient may have had more than one associated type of congenital anomaly the sum in this table is greater than the total number of cases with associated congenital anomalies.

incidence of urinary infections when the condition is not taken care of. When there was a congenital stricture of the rectum and anus it was usually found 2 to 4 cm. from the anus, up to the level of the mucocutaneous junction. According to David,[16] this stricture is actually composed of mucosa and submucosa, but is often mistaken for spasm of the sphincter muscle.

The methods of treatment used in the 165 cases are given in Table VI according to the type of anorectal anomaly present. All of those in type I were treated by dilatation only and, at the time of dismissal, all had a satisfactory result. Thirty (48.4 per cent) of the 62 patients of type II underwent incision and dilatation of the anus at the clinic or elsewhere. Six of this group underwent proctoplasty with dilatation, and 10 underwent colostomy. Eleven females of this group had only a dilatation of the rectal fistula, and another 11, who had normal bowel movements through a rectovaginal fistula, did not receive treatment at the time they were seen. They were told to return later for plastic procedures on the vagina and rectum.

TABLE VI. SUMMARY OF METHODS OF TREATMENT USED

	TOTALS*		TYPES I AND IV		TYPE II		TYPE III	
TREATMENT	NUMBER	PER CENT OF 165 CASES	NUMBER	PER CENT OF THOSE TYPES OF CASES	NUMBER	PER CENT OF 62 CASES	NUMBER	PER CENT OF 95 CASES
Dilatation only	4	2.4	4	All of type I	0	0	0	0
Incision and dilatation	30	18.2	0	0	30	48.4	0	0
Proctoplasty with dilatation	70	42.4	2	50.0 of type IV	6	9.7	62	65.3
Unsuccessful perineal exploration	13	7.9	1	25.0 of type IV	0	0	12	12.6
Colostomy	65	39.4	2	50.0 of type IV	10	16.1	53	55.8
Plastic operation on fistula	51	30.9	2	50.0 of type IV	14	22.6	35	36.8
Dilatation of fistula	16	9.7	0	0	11	17.7	5	5.3
Fistula open, no treatment	13	7.9	0	0	11	17.7	2	2.1
Colectomy with ileostomy	1	0.6	0	0	0	0	1	1.1

*Since a patient may have had more than one method of treatment, the sums in this table are greater than the total number of cases.

Sixty-two (65.3 per cent) of the 95 patients of type III underwent proctoplasty with dilatation of the anus. As mentioned previously, 12 underwent unsuccessful perineal exploration. Fifty-three of the group (55.8 per cent) underwent colostomy. One patient, a girl of 6 years, had colectomy of a huge megacolon and an ileostomy made elsewhere.

Thus 65 (39.4 per cent) of the 165 patients underwent colostomy. Forty-nine (57.6 per cent) of the males and 16 (20 per cent) of the females underwent colostomy. Of the 65 patients who underwent colostomy, in 19 of the males and 3 of the females "distal-loop trouble" developed. This means that 33.8 per

TABLE VII. DISTAL-LOOP TROUBLE AMONG CASES IN WHICH COLOSTOMY WAS PERFORMED

SEX	CASES WITH COLOSTOMY	CASES WITH DISTAL-LOOP TROUBLE	
		NUMBER	PER CENT
Male	49	19	38.8
Female	16	3	18.8
Total	65	22	33.8

cent of the patients undergoing colostomy had some difficulty related to the distal loop. Tables VII and VIII give the incidence and the various types of difficulty which developed in the distal loop of the stoma.

As might be expected, the most common difficulty was impacted feces, occurring in 10 of the 22 patients. Of these 22, 11 had conditions which could have been prevented or at least lessened by a careful separation of the proximal and distal colostomy loops at the time of the initial operation. We should like to present the case of a patient who illustrated the seriousness of this condition. He was the only one of the 165 who had any family history of anorectal anomaly. His mother and one sister had both been born with rectal strictures which were treated by dilatations. Two patients of the 165 had cousins who were reported to have a congenital anomaly. One cousin had a harelip, and in the other case the type of anomaly was not mentioned in the patient's record. Of the 165 patients, 3 were twins. In each instance, the other twin was said to be normal. One set of twins was said to be identical, one set was questionably identical, and the third set consisted of fraternal twins.

TABLE VIII. NATURE OF THE DISTAL-LOOP TROUBLE

TYPE	MALE	FEMALE	TOTAL
Impacted feces	8	2	10
Barium concretion	3	0	3
Calculus of urinary origin	1	0	1
Prolapse of distal barrel	7	1	8
Retraction of distal barrel	2	0	2
Urine dribbled out of distal loop	3	0	3
Total number with trouble	19	3	22

REPORT OF CASE

The patient was first seen at the clinic, Nov. 7, 1929, at the age of 3½ years. His mother stated that colostomy had been performed shortly after his birth. The results of physical examination at the clinic were essentially normal except for the finding of an imperforate anus and a colonic stoma in the right flank. The patient never had had any symptoms of a recto-urinary fistula and no evidence of any was found. Also there was no evidence of other congenital malformations. The child was sent home and his mother was advised to bring him back for a perineal exploration when he was older. Because the family did not want any further surgical intervention the patient was not seen until July 6, 1948, when he returned of his own accord at the age of 23 years. His main complaint was the presence of a large, hard mass in the lower part of the abdomen. Other than pneumonia, at the age of 5 years, followed by empyema which was treated by drainage of the right side of the chest, and an appendectomy at the age of 12 years, he had been fairly well. However, he was having colostomy movements only every seven to ten days and then only after taking 1 to 1½ fluid ounces (about 30 to 45 c.c.) of castor oil.

Physical examination showed him to be fairly well developed but he appeared younger than the stated age of 23 years. He was 5 feet 8 inches (about 173 cm.) in height and weighed 147 pounds (about 67 kilograms). An apical systolic murmur was heard, but a definite diagnosis of congenital heart disease could not be made. The blood pressure on initial examination was 170 mm. of mercury systolic and 70 diastolic, but on subsequent examinations it was 130/70. Above the symphysis was a very large, hard mass which was thought to be stool in the distal loop of the pelvic colon. Although the anus appeared to be imperforate, and its normal site was evidenced only by a longitudinal band of tissue about 1 cm. in diameter and 4 cm. in length, apparently there was a fistulous communication between the end of the distal loop of the colon and the perineum, because the patient stated that he could squirt water into the colonic stoma and recover some of it on the perineum. Proctoscopic examination on July 7 showed the proximal loop of the stoma to be normal for a distance of 20 cm. The distal loop of the stoma was examined for a distance of 12 to 14 cm. There was a large, hard ball of stool at the lower limit of the segment examined. The anus seemed to have sphincter muscle present but was imperforate. A roentgenogram of the abdomen made on July 9 showed a large fecal mass containing radiopaque material.

The patient returned home for a few weeks and then on August 10 one of us (C. W. M.) performed a transsigmoidal removal of a fecal impaction, and excision of the sigmoid and lower part of the descending colon. The operative diagnosis was congenital absence of the rectum and anus with fecal impaction in the sigmoid. A primary lower left rectus incision was made, the rectus muscle being retracted laterally. The colonic stoma made soon after birth seemed to be in the descending colon just below the splenic flexure. The large mass which had been seen roentgenographically and had been palpated was in the distal portion of the sigmoid. The bowel ran down to the rectosigmoid, where it was strictured. There was no demonstrable opening into the rectum, but there was a densely scarred area at this point. Because of the huge distention of the bowel resulting from the fecal impaction in the blind end of the sigmoid, the impaction had to be removed through a transsigmoidal incision by scooping the material out with the fingers and scoops. There was enough hard fecal material to fill a quart jar. This material had distended the bowel greatly so that it was difficult to dissect out the sigmoid. The sigmoid was dissected to within 2 to 2½ inches (about 5 to 6 cm.) from the colonic stoma, where a Payr clamp was placed on the distal loop and the upper stump of the distal loop was inverted over the clamp. The portion of the bowel between the clamp and the termination of the bowel in the rectosigmoid was removed. Because there was no rectum the prostate was displaced back against the lower part of the sacrum. Sulfanilamide, 10 Gm., was left in the abdominal cavity and two Penrose drains were brought out through the lower end of the incision.

The pathologist's report was as follows: The specimen contained 15 cm. of rectum and rectosigmoid, and also material from the rectum. There was an impacted mass of feces in pieces approximately 12 cm. in diameter. The mass was impregnated with calcium. The rectal wall showed mild inflammatory changes in the mucosa with fibrosis of the muscle near the anus.

The patient's postoperative course was complicated by peritonitis and ileus which responded to the use of Miller-Abbott tube suction and the administration of neostigmine. The drainage at the site of the Penrose drains became profuse and purulent. On the nineteenth postoperative day a penicillin solution, which was injected along the site of the Penrose drains, was noted to be leaking out of the distal loop of the colonic stoma. Hence, on August 26 a plastic procedure was done on the stoma by one of us (C. W. M.). The incision was made below the previous stoma. The lower segment of the stoma, which had been inverted about 1½ inches (about 4 cm.) below the primary stoma, was brought up. The anterior wall of the distal stump was incised, and the stump was connected with the previous stoma. After this procedure the patient's course was uneventful and he was dismissed from the hospital on the fifth day after the plastic procedure on the site of colostomy. A letter from him on September 28 stated that the colostomy movements occurred daily each morning without the use of any laxatives. The drainage at the lower end of the right rectus incision

had completely ceased. He had gained fifteen pounds (about seven kilograms) in three weeks and was feeling very well. This patient was considered as having a satisfactory result of treatment.

RESULTS

In evaluating our results we tried to give the consultant's clinical impression at the time of the patient's dismissal. A result was said to be good if the patient had either no fistula, or one successfully treated, and had control of normal bowel movements through the perineal anus. To be considered a satisfactory result the patient had a satisfactorily functioning colonic stoma or control of a perineal anus and no symptoms from a fistula, if the latter were present. Those patients listed as having fair results had only fair control of bowel movements and several had occasional symptoms from the fistulas. A patient with a poor result was incontinent of the usual bowel movement, and usually had a urinary fistula which dribbled urine out through the incompetent anus. In caring for these patients we feel that our goal is primarily a satisfactory method of defecation and urination with control and separation of the urine and feces. Anatomic correction of the malformation is of secondary importance. We agree with Bailey and Love[17] that "a colostomy is preferable to an incontinent anal orifice in the natural position."

TABLE IX. RESULTS OF TREATMENT (ACCORDING TO SEX)

RESULTS	TOTAL		MALES		FEMALES	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Good	15	9.1	2	2.4	13	16.3
Satisfactory	68	41.2	40	47.1	28	35.0
Fair	40	24.2	16	18.8	24	30.0
Poor	27	16.4	16	18.8	11	13.7
Hospital deaths	15	9.1	11	12.9	4	5.0

The results of treatment of the 165 patients are summarized in Tables IX and X. Of the males 49.5 per cent and of the females 51.3 per cent, or about one-half of the patients were considered to have a good or satisfactory result at the time of dismissal. Of the males 37.6 per cent and of the females 43.7 per cent had only a fair or a poor result on dismissal. Many of these patients are coming back for definitive treatment after they are older. Among the 165 patients there were 15 hospital deaths (9.1 per cent), 4 of which were due to an associated congenital anomaly and not to the imperforate anus. Crowell and Dulin[9] reported 65 per cent satisfactory results in their series with a mortality

TABLE X. RESULTS OF TREATMENT (ACCORDING TO TYPE)

RESULT	TYPE I		TYPE II		TYPE III		TYPE IV	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Good	0	0	7	11.3	8	8.4	0	0
Satisfactory	4	100.0	25	40.3	37	38.9	2	50.0
Fair	0	0	22	35.5	17	17.9	1	25.0
Poor	0	0	6	9.7	20	21.1	1	25.0
Hospital deaths	0	0	2	3.2	13	13.7	0	0

rate of 17 per cent. Friedmann[18] in 1944 gave the mortality rate of colostomy for imperforate anus as 50 per cent. Twelve of the 65 patients who underwent colostomy died, a colostomy mortality rate of 18.5 per cent.

When the results of treatment by types of anorectal anomaly are studied, it is found that 51.6 per cent of type II and 47.3 per cent of type III had satisfactory or good results. One would expect to find more poor results (21.1 per cent) among the patients in type III than among patients of type II because of the nature of the deformity, a rectum fairly widely separated from the proctodeum.

In evaluating the results of treatment and the various types of anorectal anomalies it was difficult to get a true picture of the real incidence of each type. It is known that many babies are treated by their local physician and never require later care. Also, several of the patients, in fact the large majority, had their primary treatment elsewhere, and were not seen at the clinic until some complication had developed. One patient had four colostomies, three attempts at repair of a rectovesical fistula, and two proctoplasties. It is difficult to obtain a satisfactory result in the patient who has "shopped around" to three or four different surgeons and not allowed any one of them to complete a program of treatment.

The causes of death in the 15 of the 165 patients are listed in Table XI. The deaths were all hospital deaths. Eight of the 15 were directly related to the imperforate anus. Four of the 15 were due to associated congenital anomalies. One was due to bronchopneumonia, one to atelectasis, and one to pyelonephritis.

TABLE XI. CAUSES OF DEATH

CAUSE	NUMBER	PER CENT
Chronic intestinal obstruction	3	20.0
Peritonitis	3	20.0
Bronchopneumonia (2 had tracheo-esophageal fistulas)	3	20.0
Shock after colostomy	2	13.2
Tracheoesophageal fistula	1	6.7
Pyelonephritis	1	6.7
Congenital heart disease	1	6.7
Atelectasis	1	6.7

SUMMARY

One hundred sixty-five patients having anorectal malformation were studied with special reference to the sex incidence of the condition, the type of the anomaly, the incidence of fistula formation, the incidence of associated congenital anomaly, the method of treatment, and the results of treatment.

There were 85 males and 80 females, of whom 70.6 per cent and 95 per cent, respectively, had rectal fistulas. Of the males 51.8 per cent and of the females 36.3 per cent had some associated congenital malformation present.

Sixty-five of the patients (39.4 per cent) underwent colostomy, of whom 22 (33.8 per cent) had distal-loop trouble. A case illustrating the nature of this trouble is presented.

Of the patients, 50.3 per cent had good or satisfactory results and 40.6 per cent had fair or poor results. There was a hospital mortality rate of 9.1 per cent.

In conclusion we wish especially to emphasize the importance of (1) early colostomy in the male with evidence of type III imperforate anus with recto-urinary fistula; (2) separation of the distal from the proximal loop of the colonic stoma in all cases in which colostomy is the preferred method of treatment.

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SEPARATE CARCINOMAS OF RECTUM AND PROSTATE WITH RESECTION OF PELVIC VISCERA AND EXTERNAL GENITALS

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COMPLETE resection of the pelvic organs for separate carcinomas of the rectum and of the prostate is very rare. A search of the literature and of the records at the Presbyterian Hospital fails to reveal a similar case in which the rectum, bladder, prostate, and external genitals (Figs. 1 and 2) have been removed for this dual pathology. Recent personal communications from several of the leading surgeons in the United States specializing in colon and rectal surgery did not disclose another case of this kind. A communication from McKittrick[7] stated that one of his patients presented a carcinoma of the rectum and a separate carcinoma of the prostate, in which an abdominoperineal resection of the rectum with perineal prostatectomy was done.

Scott[9] stated that the records of Strong Memorial Hospital show only two coexistent primary carcinomas of the rectum and prostate and that the diagnoses were made at autopsy. These were the only two in a series of 9,000 careful autopsies.

In a careful study of about 800 cases of carcinoma of the prostate, Young[10] stated that the rectal mucosa had been invaded and ulcerated in not over a dozen cases. In no instance did he refer to the coexistence of carcinoma of the rectum as a separate entity in these cases.

Likewise, Nesbit and Plumb[8] in 1946 reported an analysis of 795 cases of carcinoma of the prostate without making any reference to the coexistence of carcinoma of the rectum.

It is well known that about 70 per cent of the carcinomas of the large bowel occur within reach of the sigmoidoscope and that 50 per cent of those involving the large bowel are within reach of the examining finger. The diagnosis is usually easily made by palpation and by sigmoidoscopic examination, and can be easily confirmed by biopsy.

Young[10] stated that carcinoma of the prostate occurs in 14 per cent of all men over 44 years of age, and that it is three times as common in men as carcinoma of any other internal organ. In 1948 McCaffery and Hess[6] reported a study of 1,100 cases of prostatic enlargement, 197, or 17.09 per cent, of which were diagnosed clinically as carcinoma.

The earliest clinical diagnosis of carcinoma of the prostate is based upon finding, on rectal examination, a cartilaginous or stony hard nodube in the posterior lobe of the prostate. This must be differentiated from a calculus, long-standing prostatitis, infarct, or tuberculosis. Often only a biopsy can settle the diagnosis.

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Kutscher and Wolbergs[5] in 1935 discovered that normal human prostatic tissue is extremely rich in "acid" phosphatase. Further studies of this enzyme lead to the development by Gutman[2] of a chemical method for the diagnosis of metastasizing prostatic carcinoma, and to the introduction by Huggins[3] in 1941 of androgen control, an important new principle in the treatment of carcinoma of the prostate.

In association with the stony hard mass, an elevated serum acid phosphatase, as described by Gutman, above 3 or 4 units per 100 c.c. of serum, is suggestive of the metastasis or extension of the carcinoma of the prostate outside of the capsule, although this elevated value is not pathognomonic of metastases from carcinoma of the prostate.

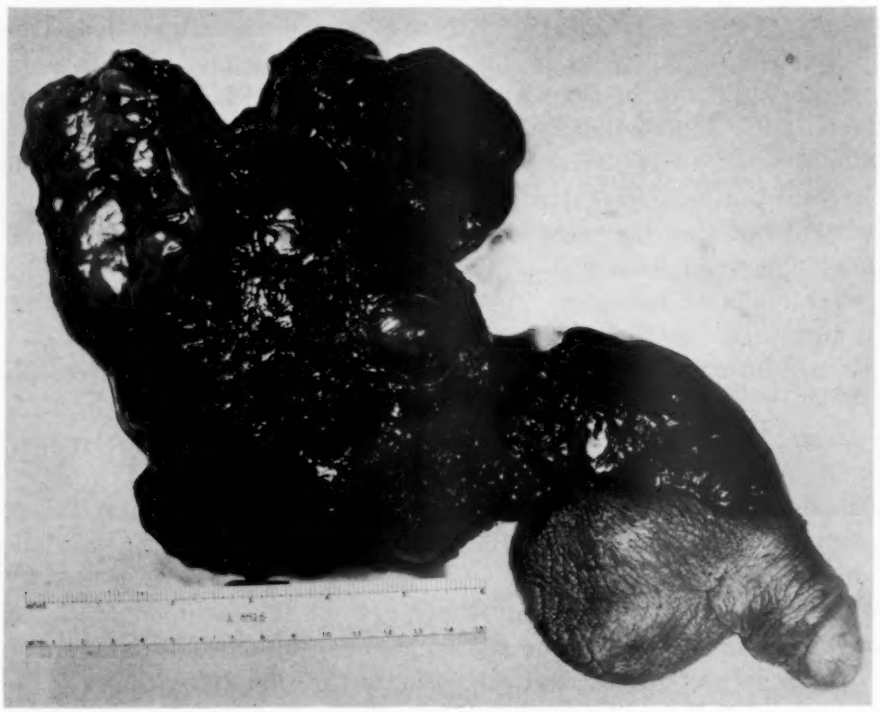


Fig. 1.—Gross specimen showing external genitals, bladder, and prostate to the right, and the distended rectum to the left.

Carcinoma of the rectum, in the light of our present knowledge, can be cured only by sufficiently radical surgical extirpation. Radium and x-ray therapy are of little or no curative value.

By the same principle carcinoma of the prostate cannot be cured by other than sufficiently radical surgical means, even though orchectomy and the administration of diethylstilbestrol (androgen control, as introduced by Huggins in 1941) are very valuable in providing comfort and prolonging life. Transurethral resections of the prostate have been done frequently for relief of urinary obstructive phenomena resulting from carcinoma of the prostate, but this cannot be relied upon to extirpate completely carcinoma of the pros-

tate. Of all the procedures which have been suggested by the urologists, radical perineal prostatectomy seems to offer the greatest hope of cure, even though this procedure, as advocated and practiced by Young, has not been enthusiastically followed by urologists generally.

Pelvic glands were palpated in about 20 per cent of Young's cases of carcinoma of the prostate. In a careful study of 100 autopsies of patients who died of carcinoma of the prostate, Kaufman[4] discovered involvement of the pelvic glands in twenty-seven cases.

Metastases are found most commonly in the bones of the pelvis, spine, and femur. These apparently are disseminated much more commonly through the blood stream than through the lymphatics, even though the more recent work by Kahler has shown that perineural lymphatics may be involved very early.

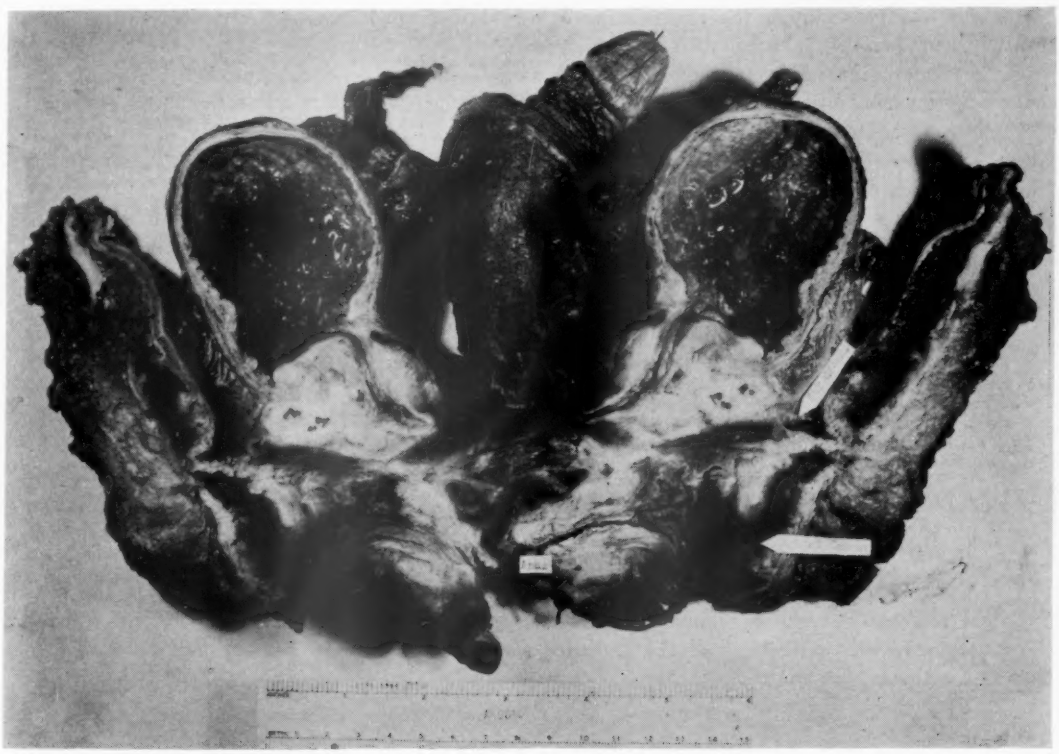


Fig. 2.—Gross specimen bisected, showing external genitals in the center, bladder on either side with the urethra surrounded by carcinoma completely replacing the prostate, and with a separate carcinoma of the rectum, indicated just below that of the prostate with the cul-de-sac just above.

About 50 per cent of the patients in whom radical resection of carcinoma of the rectum has been done are alive and free of metastases or evidence of recurrence five years following operation.

Young stated that, following radical prostatectomy, about 50 per cent of his patients with carcinoma of the prostate, followed five years or more, showed no evidence of recurrence or metastases.

CASE REPORT

H. R. (No. 915095), a 62-year-old laundry worker of Russian descent, was admitted to the Presbyterian Hospital because of difficulty in starting the urinary stream for some six to eight months, associated with marked frequency and straining on urination, with the passing of stool each time the urine was expelled. Bood had been noted in the stool about once a month for the preceding year and mucus had been seen in the stool during the past six months. Occasional slight abdominal cramps were noted for a few months. There had been a loss of fifteen pounds in the past year.

Physical examination revealed a man of about 62 years of age, weighing 120 pounds, appearing chronically ill and to have lost considerable weight. Heart and lungs were normal. Liver presented three fingerbreadths below the costal margin.

Rectal examination revealed an encircling, fungating tumor of the rectum at about 8 cm. from the anal verge, typical of carcinoma. Just below this mass the prostate was extremely large, hard, nodular, and very suggestive of carcinoma. This was a separate and distinct mass from that in the rectum.

Biopsy of the rectal tumor showed an adenocarcinoma. A diagnosis of carcinoma of the prostate was based upon the presence of a very large, hard, nodular prostate, with an elevated serum acid phosphatase of 5.5 Gutman units.

Preoperative laboratory findings were as follows: acid phosphatase 5.5 Gutman units per cent (normal up to 4 units per cent); alkaline phosphatase 3.8 Bodansky units per cent; erythrocyte sedimentation rate 44 mm.; hematocrit 35.7 (–24 per cent); plasma protein 7.21 and 7.05; hemoglobin 12.6, red blood cells 4,300,000, white blood cells 10,600, neutrophils 76, leucocytes 20; electrocardiogram normal.

On x-ray examination the skeletal survey showed no definite evidence of metastases. In the chest, heart and lungs were normal; the genitourinary survey showed that the renal outlines were normal. Kidney, ureter, bladder examination showed small calcified areas suggestive of prostatic calculi.

Study by intravenous pyelogram revealed that there was some delay in excretion with a minimal degree of bilateral hydronephrosis and hydroureter. The calices and pelves were fairly well visualized, and, except for hydronephrosis, appeared to be normal.

Cystoscopy showed that the posterior urethra was tortuous and fixed. Bladder mucosa was trabeculated. An extravesical mass indented the bladder posteriorly.

Operative Procedures.—The first operation was an orchectomy. Before a more radical procedure had been decided upon, the urological service performed a bilateral orchectomy on Aug. 9, 1948. On the first postoperative day signs of superficial and deep vein thrombosis developed in the right lower leg, and anticoagulant therapy was instituted.

Transfer to the general surgical service was done when it was decided to do the more radical resection of the carcinoma of the rectum, and of the bladder, prostate, an genitals for very extensive pathology of the prostate which obstructed the urinary flow so that a retention catheter was worn constantly.

The second operation, Aug. 16, 1948, was a bilateral ligation of the saphenous veins for thrombosis.

The third operation, Aug. 24, 1948, was an abdominoperineal resection of the rectum, bladder, prostate, and external genitals, with colostomy and transplantation of ureters into the sigmoid. The operative findings and procedure were as follows.

Pathologic findings: The liver was free of any definite metastases. There were no palpable nodes in the mesentery or hollow of the sacrum. Just at and slightly above the peritoneal reflection was a tumor of the rectosigmoid which was obviously carcinoma. The prostate was extremely large. The bladder wall was greatly thickened. There was no adherence of the rectal mass to the surrounding structures. The bladder and prostate were not abnormally fixed.

Procedure: The abdomen was entered through a low left-rectus splitting incision. The site of the colostomy was established in the lower sigmoid. From this point the right leaf of the mesentery was incised down into the pelvis and, through finger dissection, mobility

of the tumor mass and bladder was established. This peritoneal incision was carried up over the right side of the pelvis to the right of the bladder and a similar incision was made on the left side. The bladder was completely freed anteriorly. The superior hemorrhoidal vessels were clamped, incised, and ligated with No. 1 chromic catgut. The lower mesosigmoid vessel was not incised. There were no nodes encountered. The vesical arteries and veins were incised and ligated with No. 1 chromic catgut. The lateral ligaments were incised and the rectum, bladder, and prostate were separated from the surrounding pelvic walls. The ureters were isolated and incised just outside the bladder wall bilaterally. The distal sigmoid was incised between silk ligatures. Each end was covered with a rubber dam. The distal segment was dropped into the pelvis.

Ureteral transplant: At a point some 20 cm. from the distal end of the proximal segment an opening was made into the gut on the mesenteric surface about 1 cm. in diameter. The end of each ureter was incised about ½ cm. so as to increase the size of the opening and expose the mucosa. Silk 000 was placed through the periureteral tisue at the end of the ureter and a suture of atraumatic chromic catgut was placed in the submucosal tissue at the end of each ureter. Both ureters were drawn through the opening into the gut and fixed about 2 cm. from the gut opening by carrying all of these sutures through the gut wall and tying them about 1 cm. apart. The edge of the sigmoidal mucosa was sutured to the ureteral walls so as to obtain a complete closure around both ureters without constriction. The adjacent peritoneal edges were sutured to the gut over the anastomosis so as to cover and fix the anastomosis completely. There was no tension in the region of the anastomosis. No attempt was made to reconstruct the peritoneal floor.

Ureteral closure: Using No. 30 gauge interrupted double figure-of-eight wire sutures through the external fascia and peritoneum the incision was closed. Skin was approximated with continuous 000 silk.

Perineal procedure: The anus was closed with heavy silk. An incision was made beginning well above the base of the penis and extending posteriorly bilaterally around the base of the scrotum and encircling the anal region. By deepening this encircling incision the penis, scrotum, and rectum were separated from the surrounding structures. This dissection was carried upward into the pelvis to continue separation so that the entire specimen consisting of lower sigmoid, rectum, bladder, prostate, penis, scrotum, and anal region was removed en masse (Figs. 1 and 2). When the specimen was removed the small intestinal loops could be seen hanging in the pelvis.

Perineal closure: With No. 32 gauge wire, the skin and subcutaneous tissue were approximated over the posterior three-quarters of the wound. The anterior one-quarter was closed with interrupted 000 silk.

Gross.—The specimen consisted of a single block of tissue composed of a piece of large bowel which included in the contracted state the distal 23 cm. of the large bowel, the anus, and 3 cm. of the surrounding skin, with the bladder, prostate, penis, remnants of the spermatic cords, and the scrotal sac (Figs. 1 and 2).

Six centimeters above the mucocutaneous line was a circular fungating ulcerated lesion which almost completely occluded the lumen. The lesion was extremely firm and the lumen had narrowed to appoximately 1 cm. The lesion extended approximately 6 cm. along the bowel wall, and 8 cm. of uninvolved bowel was proximal to it. The rectal lesion lay at the level of the cul-de-sac and had produced a puckering of the serosal surface. There was no continuity between the rectal growth and the prostate except for a 1 cm. band of fibrous tissue 0.3 cm. in diameter. The serosa covering the bladder was smooth, shiny, and glistening, and was uninvolved by tumor. The prostate measured 5 by 4 by 3 cm. and was very firm and only slightly nodular. Posteriorly the tumor extended into the serosal fat and thirty-two lymph nodes were found, the largest of which measured 1.3 cm.

There was a marked thickening of the bladder wall along with marked trabeculation. The prostate was firm.

Microscopic.—Sections of the rectal mass revealed a glandular carcinoma (Fig. 3) characterized by large irregular glands varying markedly in size and shape and being filled with blue-staining mucoid material and occasionally pink-staining necrotic debris. The glands

were lined by large cells with abundant pink cytoplasm and contained large vesicular nuclei with hyperchromatic nuclei. There had been a loss of polarity and stratification of the cells. Mitoses averaged about 1 per 3 to 4 high-power fields. This rectal carcinoma had invaded the muscle posteriorly and almost reached the perirectal fat. Anteriorly the rectal carcinoma had extended through the muscle and invaded the perirectal fat just beneath the mesothelium of the cul-de-sac. A desmoplastic reaction accompanying the tumor accounted for the puckering noted grossly in the cul-de-sac. The anterior-inferior portion had not invaded the periprostatic tissues.

The entire prostate had been extensively replaced by an glandular tumor (Figs. 4 and 5) which was histologically distinct from the rectal carcinoma (Fig. 3), being composed of small glands and cords of epithelial cells almost completely filled by round nuclei in which the chromatin was evenly distributed through the nucleus. Nucleoli and mitoses were very infrequent. These cords and nests were separated by a fibromuscular stroma. A few small

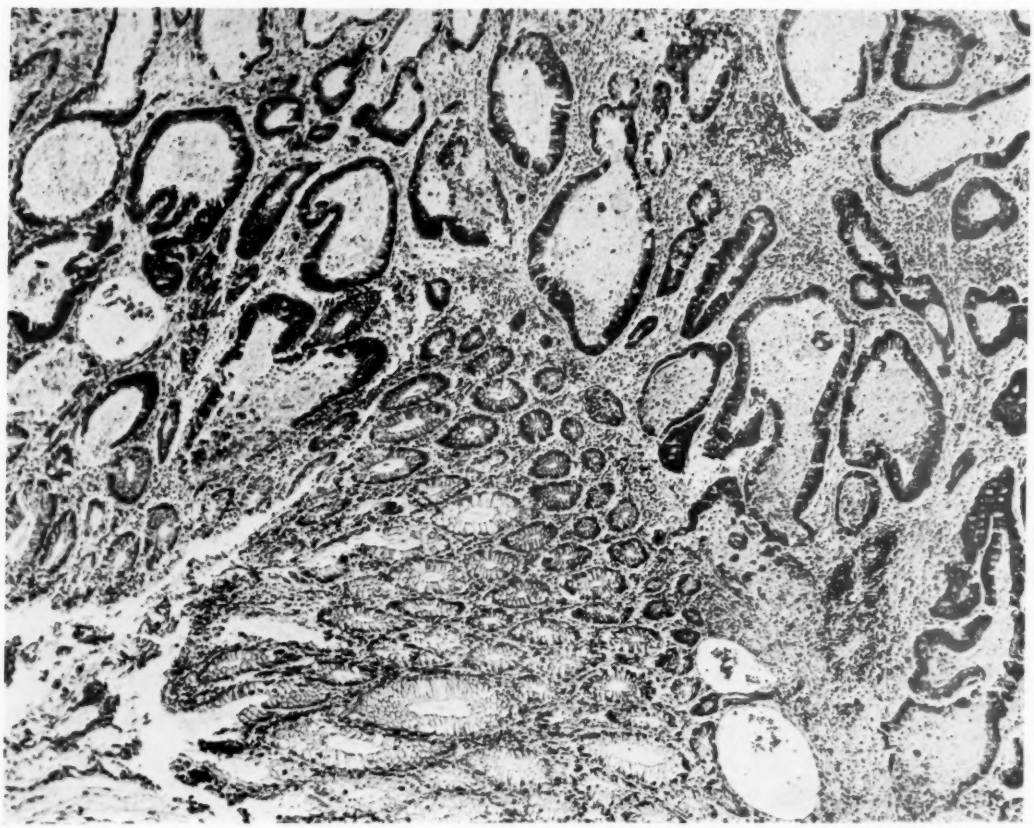


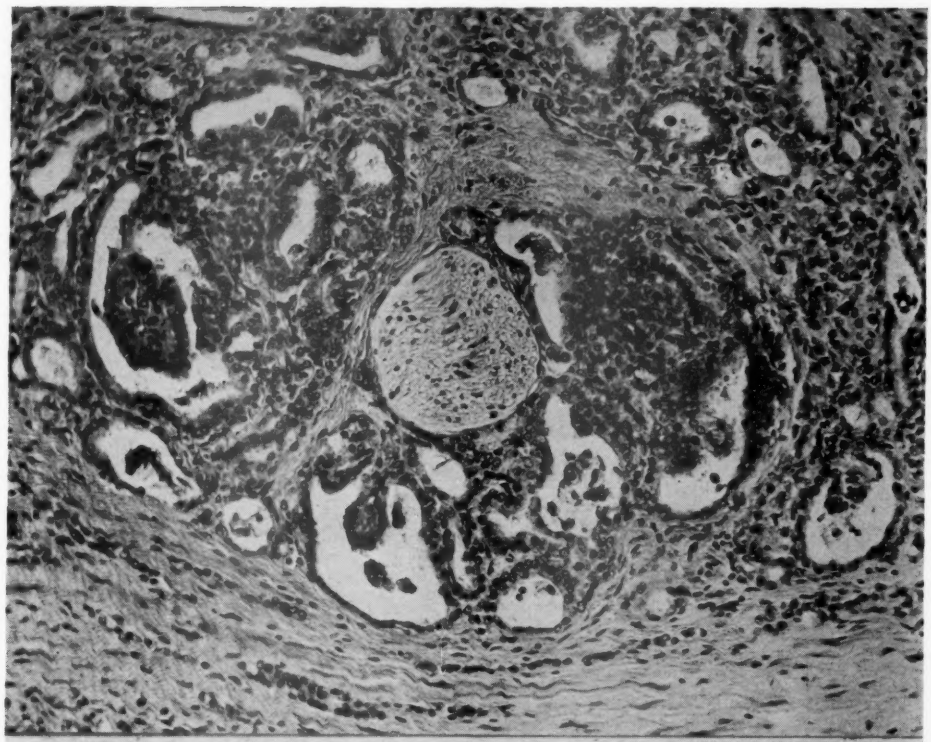
Fig. 3.—Medium-power photomicrograph of rectal tumor, showing a well-differentiated adenocarcinoma with tall columnar mucous-secreting cells.

persisting remnants of prostatic tissue remained at the periphery, filled with calcareous concretions. The prostatic carcinoma had extended beyond the capsule and could be found in the periprostatic fat, the submucosa of the floor of the bladder, and lymphatics, and into skeletal muscle in front of the prostate. All of the four nodes removed from the bladder neck were involved by prostatic carcinoma (Fig. 6). Of the twenty-eight lymph nodes found in the perirectal fat and rectum, five were involved by prostatic carcinoma (Fig. 6).

The bladder also showed considerable hypertrophy of the musculature while the stumps of the spermatic cords showed a foreign body reaction to suture material.

Diagnosis.—The diagnosis was adenocarcinoma of rectum and adenocarcinoma of prostate with metastases to the bladder and pelvic lymph nodes.

Fig. 4.



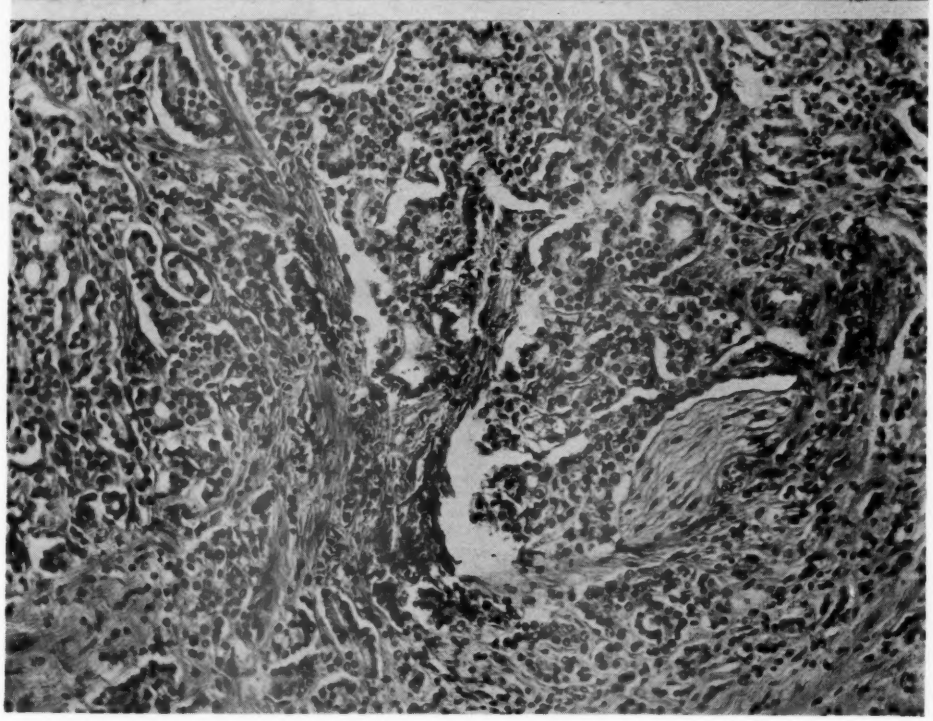


Fig. 5.

Figs. 4 and 5.—Photomicrographs (×180) showing the histologic picture of the prostatic tumor with small alveoli and papillary projections lined by cuboidal cells. The tumor cells do not resemble those of the rectal tumor. Nerve sheath invasion is evident.

Summary.—The patient had a localized rectal carcinoma which extended through the muscle but had not quite involved the serosal fat, and no metastases of the rectal carcinoma were found in the lymph nodes. The patient also had a second carcinoma which had completely replaced the prostate and invaded the capsule, periprostatic fat, and the submucosa of the bladder. Of a total of thirty-two lymph nodes, nine were involved by prostatic carcinoma.

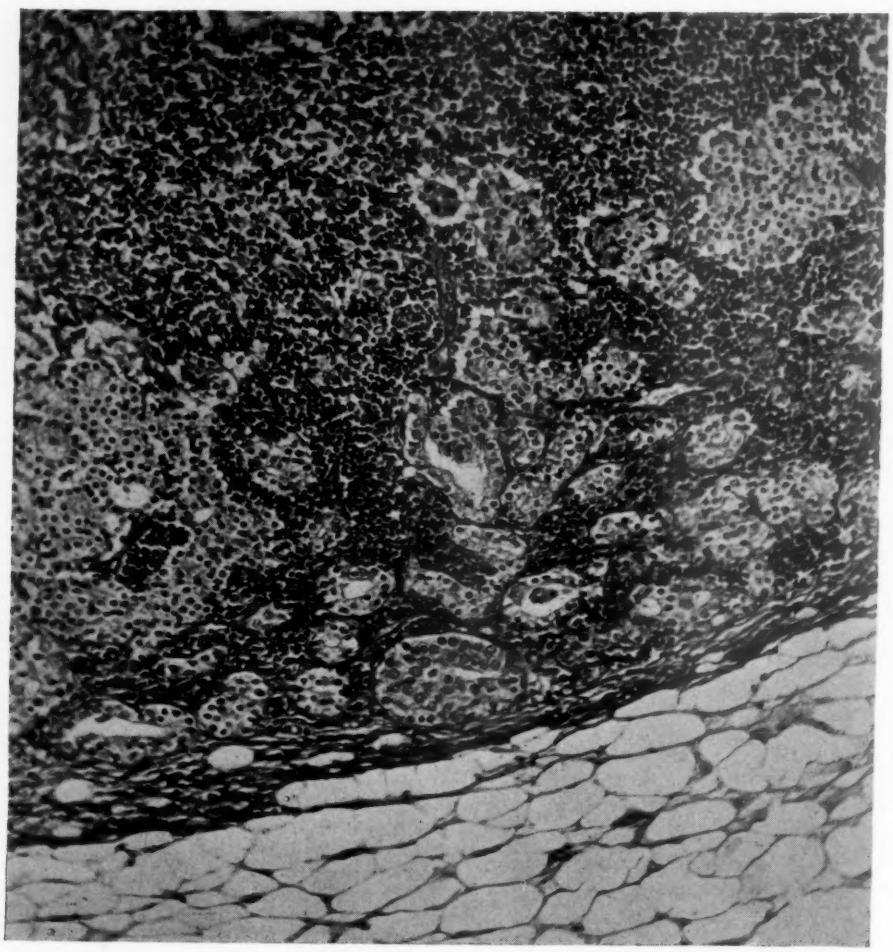


Fig. 6.—Photomicrograph (×180) showing metastases in the presacral lymph node. The tumor is identical in microscopic architecture to that found in the prostate.

Fourth Operation.—Dermatome graft was placed around the projecting colostomy limb to facilitate proper delivery of stool and urine.

Previous to the radical procedure, the patient had been prepared with transfusions, cathartics, and colon lavages daily, retention catheter for acute retention, and with sulfathalidine, 12 Gm. per day, for seven days. Anesthesia was pentothal, nitrous oxide, and curare. During the operation 3,500 c.c. of blood were given with 1,000 c.c. of dextrose in distilled water. Postoperatively Dicumarol was started on the fifth day and continued, 50 to 100 mg. per day, until the fifteenth day. Sulfadiazine and penicillin were given following the operation.

The postoperative laboratory findings were as follows. The serum acid phosphatase on the first day immediately returned to a normal of 1.1 Gutman units and remained so

during the postoperative period. The urea nitrogen on the second day was 11 mg. per cent and remained normal throughout the hospital stay. These findings were normal on discharge.

A Grick or Rutzen colostomy bag is worn extremely satisfactorily (Fig. 7). The patient is able to release the urine and stool through the lower end of the bag; he removes the bag twice a day for cleaning, and then recements it to the skin.

Fig. 7.—The patient (H. R.) eleven months after the radical resection, with a Rutzen bag cemented around the colostomy. This shows the gain of thirty-five pounds since the operation.

At follow-up examination it was found that this patient had gained thirty-five pounds, and nineteen months after the radical procedure was in excellent condition (Fig. 7). A further follow-up is, of course, indicated to

determine the value of the more radical procedure in an extremely extensive prostatic carcinoma with acute urinary retention, associated with an encircling carcinoma of the rectum with mild obstructive symptoms.

SUMMARY

A case is presented in which a carcinoma of the rectum was associated with a separate carcinoma of the prostate, without extension of the carcinoma from one organ to the other. Metastases are found most commonly in the bones of the pelvis, spine, and femur. Dissemination of metastases by blood stream are apparently much more common than by lymphatics, even though the perineural lymphatics of the prostate may be involved relatively early.

In this case the carcinoma of the prostate extended outside the capsule into the periprostatic fat, the submucosa of the floor of the bladder, the lymphatics, and the skeletal muscle in front of the prostate.

All of the four lymph nodes removed from the bladder neck were involved in prostatic carcinoma. Of the twenty-eight nodes found in the perirectal fat and in the mesorectum, five were involved in prostatic carcinoma.

No metastases suggestive of rectal carcinoma were found in the nodes.

Abdominoperineal resection of the rectum was done with removal of the bladder, prostate, and external genitals in one specimen (Figs. 1 and 2) with transplantation of both ureters through a single opening into the sigmoid loop, which was brought out through the primary left-rectus splitting incision just below the level of the umbilicus.

CONCLUSION

In view of the fact that metastases in the perirectal fat and mesosigmoid were those of prostatic carcinoma, it is strongly suggestive that a more radical procedure than has been generally used is indicated for carcinoma of the prostate, namely, an abdominoperineal resection of the rectum, with a complete removal of the bladder, prostate, and possibly the external genitals, all in one specimen. Otherwise, in the light of the pathology in this case, one cannot hope to reach a maximum of the lymphatic spread in the advanced cases. It is obvious, in this case, that simple prostatectomy with the abdominoperineal resection would not have been sufficiently inclusive to reach the involved vessels and lymph nodes. This case illustrates the necessity of radical procedures to remove as much as possible of the lymph drainage area and direct spread, for only in this way can we hope to relieve or cure the patients suffering from the more advanced lesions.

All patients having pathology of the rectum should be palpated particularly carefully for a hard nodule of the prostate which might possibly suggest carcinoma even though the coexistence of carcinoma in the rectum and prostate is very rare.

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VOLVULUS OF THE SMALL INTESTINE

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VOLVULUS of the small bowel has received relatively little attention in the North American literature. McKecknie and Priestley[9] analyzed thirty-seven cases from the Mayo Clinic in 1936, but apart from an occasional case report, no similar series has been published since. Most authors agree that volvulus is the cause of 5 to 15 per cent of intestinal obstruction. At the Royal Victoria Hospital, there have been 712 admissions for bowel obstruction in the past twenty years. Volvulus has been the etiological factor in forty-nine cases, an incidence of 6.8 per cent. In twenty-three instances, the small bowel was involved.

There are many lesions which predispose to the formation of volvulus. These are summarized in Table I. In general, it may be said that any condition which fixes one part of the bowel leaving the adjacent loop mobile may produce volvulus.

Whatever the cause, the pathology is similar in all cases. The small bowel rotates in a clockwise direction about its mesenteric axis. This results in venous obstruction, which is rapidly followed by arterial occlusion. The torsion may be intermittent at first but soon becomes fixed by edema or adhesions. Even if the mesenteric blood supply remains intact, volvulus produces a closed loop obstruction and progressive distention, and causes vascular changes in the bowel wall. The high incidence of circulatory impairment and gangrene makes this a particularly dangerous form of intestinal obstruction. In this series of twenty-three patients, the blood supply of the involved loop was impaired in sixteen cases, and resection was necessary in eight of these. The clinical manifestations of this condition are best exemplified by the following case reports.

CASE REPORTS

CASE 1.—L. M., a 59-year-old woman, had had an abdominoperineal resection for carcinoma of the rectum nine months previously. She was well until the morning of admission when she complained of the sudden onset of severe colicky pain around the umbilicus. This was followed by nausea and vomiting. The pain subsided slightly but whenever she attempted to take anything by mouth a paroxysm of pain and vomiting was initiated. About ten hours after the onset, the pain became continuous and more severe and she was admitted to the hospital. On examination, there was no abdominal distention. Muscular rigidity and tenderness were noted to the left of the umbilicus. A flat plate of the abdomen showed a distended loop of small bowel arranged in "arcade" fashion. (Fig. 1.)

A diagnosis of small bowel volvulus was made. A Harris tube was passed into the stomach and gastric suction instituted. An intravenous plasma infusion was started and the patient was taken to the operating room two hours after admission.

At laparotomy (performed by C. B. R.) a small bowel volvulus involving the terminal ileum was discovered. The bowel was bluish in color but after division of a band adhesion and detorsion, the color returned to normal. The Harris tube was then milked past the pylorus into the jejunum and the abdomen closed. Postoperatively, intestinal suction was continued for four days until peristalsis returned. The patient made an uneventful recovery.

Comment.—This case represents the typical picture of volvulus of the small intestine, so typical that the diagnosis was made on the basis of clinical and

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TABLE I. ETIOLOGY OF VOLVULUS OF THE SMALL INTESTINE

Congenital Anomalies
1. Abnormalities of rotation of the gut[7]
2. Exomphalos[2]
3. Meckel's diverticulum[11]
4. Congenital diverticula of the jejunum[10]
Acquired Lesions
1. Peritoneal adhesions[9]
(a) Postoperative
(b) Inflammatory
(c) Tuberculous
2. Internal hernia[9]
3. Foreign body impaction[4]
4. Tumors of the small bowel[8]
5. Torsion of the intestine following gastroenterostomy[13]

radiologic findings. In this hospital, a correct preoperative diagnosis has been established only four times in twenty-three cases. It is important for the surgeon to be aware that volvulus is a not infrequent cause of small bowel obstruction, and if the condition is suspected, early operation is indicated.

CASE 2.—R. L., a 40-year-old man, was in the hospital undergoing neuropsychiatric treatment for chronic alcoholism with associated polyneuritis and malnutrition. One morning he complained of crampy abdominal pain about the umbilicus and in the lower abdomen. This recurred intermittently during the day. Examination at the time revealed no abnormal findings and x-ray examination of the abdomen showed no evidence of bowel obstruction. The following day the pain was more severe and more constant and the patient complained of nausea and vomiting. He still had periods of freedom from symptoms and no definite diagnosis could be made. About forty-eight hours after the onset, his condition began to deteriorate and he went into shock. Signs of peritonitis became evident and laparotomy was performed with a preoperative diagnosis of small bowel obstruction.

At operation (by G. G. M.) practically the entire small intestine was involved in a volvulus due to pelvic adhesions. The bowel was gangrenous and twelve feet of ileum were resected. The postoperative course was febrile but with the aid of intestinal intubation, penicillin, and multiple transfusions the patient eventually recovered. During the following year, this patient was observed periodically and he remained chronically ill, a victim of malnutrition due to deficient intestinal absorption. He could not gain weight and gradually became emaciated. One year after the operation, he died. At autopsy, only three feet of small bowel remained.

Comment.—Volvulus of the small intestine may be deceptive because repeated episodes of twisting and untwisting of the bowel give rise to intermittent symptoms. In this case operation was delayed until gangrene and perforation had occurred and a massive resection was then necessary. Although only twelve feet of bowel were resected, the patient never re-established normal intestinal function. Autopsy one year later proved that the length of bowel resected is not nearly so important as the length of bowel remaining. In a similar case, three feet of ileum were resected in a 9-month-old infant; the child recovered from the operation, but died six months later of malnutrition. At autopsy, sixteen inches of small bowel remained.

CASE 3.—A. L., a 68-year-old woman, was admitted to the Royal Victoria Hospital one night with an intertrochanteric fracture of the right femur. She was prepared for operation the following morning but refused to go to the operating room because she had severe crampy lower abdominal pain. She soon began to vomit large amounts of dark, coffee-ground material which contained occult blood. Examination revealed slight abdominal distention, with tenderness in both lower quadrants. A flat plate of the abdomen showed an

arcade loop of small bowel and she was taken to the operating room immediately. Laparotomy (by C. B. R.) revealed a volvulus involving the jejunum and ileum. Several adhesions were divided and the bowel untwisted. The color, which had been purplish, returned to normal but there were many areas of thrombosis and hemorrhagic extravasation in the mesentery of the involved bowel. The intestine was returned to the abdomen and the incision closed. The postoperative course was entirely uneventful.

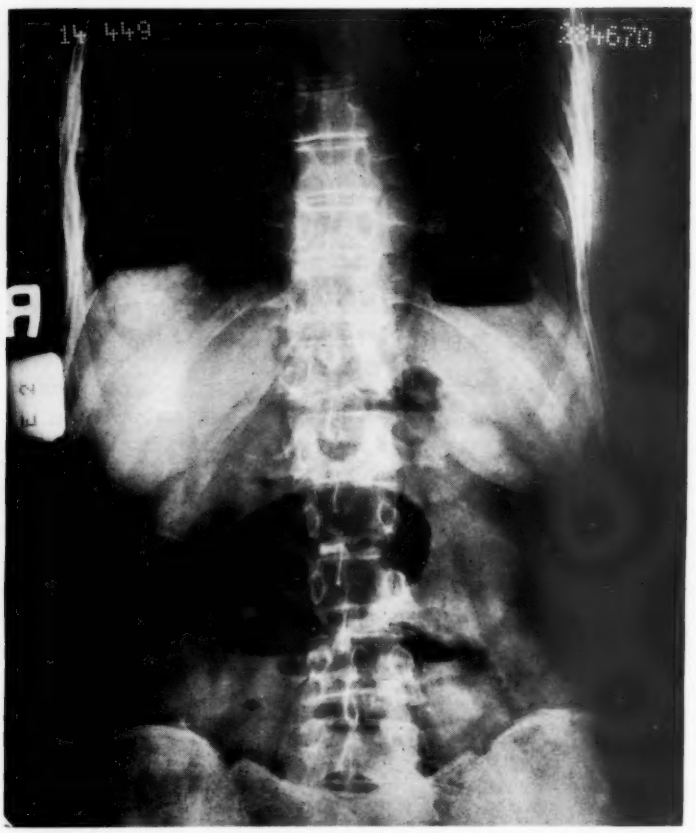

Fig. 1.—Flat plate of the abdomen in a case of small bowel volvulus (Case 1). The "arcade" loop of dilated bowel is typical of this condition.

Comment.—The symptom of hematemesis is unusual but occurred in two cases in this series. It has also been reported by Webber[14] in one patient. In both of our cases, the jejunum was involved and there was evidence of mesenteric venous obstruction. The most likely explanation of the hematemesis is that hemorrhagic extravasation occurred into the bowel lumen.

CASE 4.—C. A., a 73-year-old woman, had a subtotal gastrectomy performed for gastric ulcer. A few hours after operation, she began to complain of upper abdominal pain and nausea. Her condition deteriorated rapidly and she went into shock with clinical evidence of peritonitis. Despite supportive therapy, she died twenty-four hours after operation.

At autopsy, she was found to have a volvulus of the jejunum caused by torsion of the bowel in performing the gastroenterostomy. Gangrene had occurred and death was due to shock and intestinal obstruction.

Comment.—This unusual complication has occurred only once in more than 1,000 gastric resections performed at this hospital. In a no-loop gastroenterostomy, if the bowel is inadvertently twisted, a volvulus may result around the axis of the superior mesenteric vessels. Villafave[13] reported a similar case.

CASE 5.—V. P., a 47-year-old man, was admitted to the Royal Victoria Hospital with a history of severe colicky epigastric pain and continuous vomiting for twenty-four hours. Examination of the abdomen revealed rigidity and tenderness about the umbilicus and a flat plate showed a single distended loop of small bowel.

At laparotomy (by G. G. M.) a volvulus of the terminal ileum was found. The circulation was impaired but returned to normal after detorsion of the mesentery. The cause of the volvulus was a foreign body, half an orange, which was impacted within the bowel lumen. This was removed and the patient made an uneventful recovery.

Fig. 2.—Volvulus of the small intestine due to internal hernia (autopsy specimen).

Comment.—Foreign body as a cause of volvulus has been reported by Kerr and Kirkaldy.[4] It occurred in two cases in this series.

Peritoneal adhesions represent the most common cause of small bowel volvulus, but the condition can occur in patients who have had no previous operation and in whom no evident cause for obstruction exists. This is especially true of internal hernia and the following case affords a good example of this condition.

CASE 6.—J. H., a 78-year-old man, was admitted to hospital *in extremis* with a history of severe generalized abdominal pain, vomiting, and increasing distention of twenty-four hours' duration. Examination showed the patient to be in shock with marked abdominal distention.

Flat plate revealed many distended loops of bowel arranged in ladder pattern. He did not respond to transfusion and died on the operating table when laparotomy was performed.

At post-mortem, a strangulated volvulus of the entire ileum was found. The cause of the torsion was an internal hernia through the root of the transverse mesocolon.

DIAGNOSIS

A glance at Table II reveals that the preoperative diagnosis of small bowel volvulus is seldom made. McKecknie and Priestley found that in their series the correct diagnosis was suspected in only three of thirty-seven patients. This is not important as long as the surgeon realizes the possibility of a strangulated obstruction and the need for urgent exploration. The danger is that conservative measures may be employed for too long a period. The time element is vitally important in these cases. In this series, exploration was done in six patients within twelve hours of onset. The circulation of the bowel was impaired in three cases and there were five recoveries and one death. Exploration was done in seventeen cases more than twelve hours after onset, and in thirteen instances the circulation of the bowel was impaired. In this group, there were seven recoveries and ten deaths. It appears obvious that as time passes the incidence of circulatory impairment increases and the mortality rises.

TABLE II. PREOPERATIVE DIAGNOSIS IN TWENTY-THREE CASES OF VOLVULUS OF THE SMALL INTESTINE

DIAGNOSIS	CASES
Intestinal obstruction	13
Volvulus	4
Acute appendicitis	3
Acute pancreatitis	1
Strangulated hernia	1
Peritonitis	1

In analyzing these cases, we have found several points which should be helpful in arriving at an earlier diagnosis. A history of paroxysms of severe colicky pain associated with vomiting is suggestive of volvulus. The patient may be relatively free from discomfort in the intervals between attacks. As the process continues, the symptoms become more severe with no free periods. Abdominal distention is not prominent early, but tenderness is usual, even during a remission. Evans and Bigger[3] have pointed out that when a strangulating obstruction is present, the patient is apt to be uncomfortable when supine and seeks a "position of relief" which avoids traction on the mesentery. This phenomenon has been observed in several of our cases and appears to be a valuable sign.

The radiologic findings may be deceptive, but in about one-half the cases, the arrangement of distended small bowel loops in "arcade" pattern is suggestive of volvulus.[6] In other instances, the picture is indicative of small bowel

TABLE III. EFFECT OF TIME INTERVAL ON PROGNOSIS IN VOLVULUS OF SMALL INTESTINE

DURATION	NUMBER OF CASES	IMPAIRED CIRCULATION	RECOVERED	DIED
Operation within 12 hours	6	3	5	1
Operation after 12 hours	17	13 (7 gangrene)	7	10
Total	23	16	12	11

obstruction with multiple dilated loops and fluid levels. Rarely, as in Case 2, the x-ray may be negative in the early stages. With these criteria, it should be possible to suspect the correct diagnosis in at least one-half the cases and establish the need for urgent laparotomy in most of the remainder.

TREATMENT

The importance of early operation cannot be too strongly emphasized. As soon as shock has been combated and fluid and electrolyte loss replaced, exploration is indicated. We do not feel that attempts to pass an intestinal tube are justified. Manipulation of the patient under fluoroscope consumes valuable time which is better spent in transfusion and fluid replacement. We have adopted the practice of passing a Harris tube into the stomach and employing continuous gastric suction during the preoperative period. At laparotomy, after detorsion of the volvulus, the tube can be milked through the pylorus to the site of the dilated loop, and intestinal decompression can then be utilized as a postoperative measure. Since most deaths result from shock and infection, the indications for transfusion and antibiotic therapy are clear. With early diagnosis and modern supportive measures the mortality from this condition should be greatly reduced.

SUMMARY AND CONCLUSIONS

1. Volvulus of the small intestine is not as rare as has previously been reported. It probably represents the commonest type of volvulus seen on this continent.

2. The diagnosis should be suspected in many cases on the basis of clinical and radiologic findings.

3. Circulatory impairment is frequent in the involved loop.

4. Delay in operation increases the possibility of gangrene and the subsequent mortality.

5. The treatment of choice is early laparotomy as soon as shock has been treated and fluid and electrolyte balance have been restored. The type of operation depends upon the findings. In many cases, detorsion and correction of the causative abnormality is all that is necessary. If gangrene has occurred, resection and primary anastomosis are preferable to exteriorization of the involved bowel.

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ACUTE PANCREATITIS WITH HYPERLIPEMIA

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THE association of hyperlipemia with acute pancreatitis is not generally recognized in the surgical literature. Two patients with this combination of conditions have been studied recently on the surgical wards of the Duke Hospital and are the subject of this report. Both entered the hospital as surgical emergencies with acute abdominal pain. Both had milky blood serum from increase in blood fats. Both developed hyperglycemia, glycosuria, and ketonuria. In both, the hyperlipemia disappeared as the attack subsided and carbohydrate metabolism was brought under control with insulin. One had an eruptive form of xanthomatosis. The other developed evidence of a lower nephron nephrosis. Both survived under a conservative regime of treatment which included large doses of insulin, continuous suction drainage of the stomach, transfusions, and maintenance of fluid and electrolyte balance.

CASE REPORTS

CASE 1 (A 17674).—H. G. H., a 34-year-old white man, a taxi driver, was admitted as an emergency patient at 12:30 A.M., April 19, 1948, with a three-hour history of constant excruciating mid-epigastric pain which radiated through to the back and was accompanied by nausea and vomiting. He had had two similar though much less severe attacks five weeks and one week previously which he had attributed to constipation, as each attack was relieved after a day or two when he passed gas by rectum. He noticed the appearance of yellowish skin lesions on the knees, buttock, and posterior surface of thighs about the time of the first pain five weeks previously.

His past health had been excellent and he had never had digestive difficulties before this present illness. He had been discharged from the Navy without physical impairment in 1945. In 1947 sugar was found in the urine when he tried to enlist in the Army. He had had no symptoms of diabetes and had not been under treatment for the glycosuria. He denied excessive use of alcohol, though he said he had been a moderate drinker for years.

On examination the rectal temperature was 37.8° C. (100° F.), pulse was 80, respirations were 20, and blood pressure was 150/90. He was obese, appeared acutely ill, and complained bitterly of epigastric and back pain. The abdomen was not distended. There was marked tenderness with rebound tenderness over the entire upper abdomen most marked in the epigastrium. There was no muscle spasm. The liver edge was palpable 2 cm. below the right costal margin. It was not tender. No intestinal peristalsis was heard. There were numerous 5 by 5 mm. xanthomatous lesions scattered over the body. Clusters of larger lesions were present over the buttock and extensor surface of the thighs and forearms. The remainder of the physical examination including ophthalmoscopic examination was normal.

Our attention was immediately directed to his hyperlipemia when blood drawn on admission for routine studies showed a milky white serum as soon as it had clotted (Fig. 1). Laboratory studies subsequently were reported as showing a 4 plus serum amylase, no elevation in serum lipase, blood sugar 320 mg. per cent, CO_2 combining power 49 volumes per cent, total cholesterol 760 mg. per cent, calcium 7.9 mg. per cent, phosphorus 5.6 mg. per cent, alkaline phosphatase 3.8 Bodansky units. The hemoglobin was 16.5 Gm. per cent, white blood cells, 12,320 with 79 per cent segmenters, 8 per cent stabs., 1 per cent juveniles, 7 per cent eosinophils, and 5 per cent lymphocytes. The urine showed a 1 plus sugar, 1 plus acetone, no albumin, and an occasional granular cast. The hematocrit was 42. A sedimentation rate by Wintrobe method was 39 mm. in one hour.

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A diagnosis of acute pancreatitis with hyperlipemia and hyperglycemia was made. He was put on continuous suction stomach drainage, intravenous fluids, and insulin. He never developed signs of circulatory collapse. For the first seventy-two hours he continued to have glycosuria and acetonuria, although he received 335 units of regular insulin. Temperature rose to 39° C. about fifteen hours after admission and gradually returned to normal during the next four days. The abdominal pain became diffuse and he developed signs of generalized peritoneal irritation during the first hospital day. This subsided over the next four days. The serum lipase was normal on the first and fifth day of the illness. The blood amylase had returned to normal by the third hospital day. One of the skin lesions was biopsied on the eighth hospital day and was reported as xanthoma diabeticorum. During the eighteen days of his hospital stay the serum cholesterol dropped from 760 to 280 mg. per cent. His insulin requirement dropped to 25 units of protamine zinc insulin daily. The serum calcium rose to 10.1 mg. per cent, and the phosphorus dropped to 3.9 mg. per cent. Bromsulfalein study showed 30 per cent retention at the end of five minutes with no retention after forty-five minutes. Barium studies of the stomach and duodenum were normal. Intravenous urograms and gallbladder series were also normal.

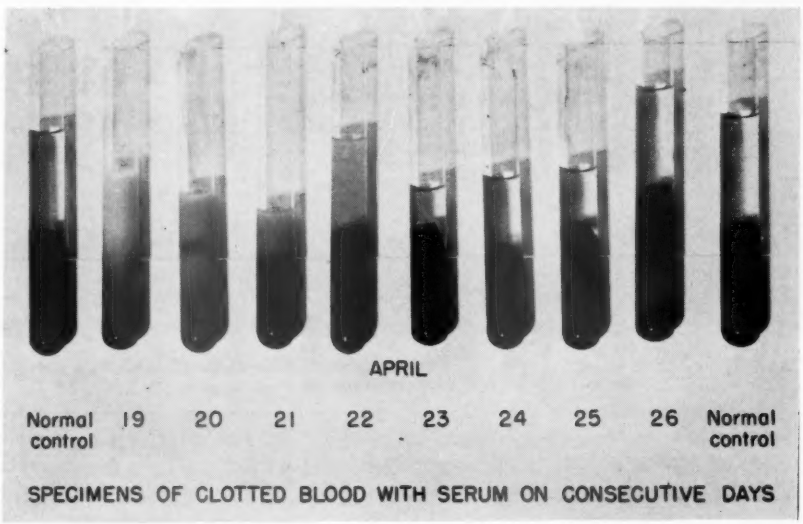

Fig. 1 (Case 1).—Appearance of blood samples taken from patient on consecutive days. The serum was milky during the first four days.

The serum, which was milky white on admission, gradually cleared (Fig. 1), and after the fourth day there was no evidence of lipemia. The xanthomatous lesions of the skin had almost completely disappeared by the time of his discharge on the eighteenth hospital day.

Ten days after discharge from the hospital he had another attack of severe mid-epigastric pain. This attack lasted only about four hours, and he never developed any signs of peritoneal irritation.

We have followed this patient regularly as an outpatient for six months. The diabetes has been well controlled with diet and insulin, and he now requires only 20 units of protamine zinc insulin daily. He has had no further pain and his general health has been excellent. Serum cholesterol has remained around 275 mg. per cent.

CASE 2 (A 34413).—A. B. C., a 48-year-old white man, a farmer, was admitted as an emergency patient at 3:30 A.M., Dec. 5, 1948, because of a twelve-hour episode of abdominal pain which had become agonizing in the preceding two or three hours. Pain was upper abdominal and radiated to the back. It was continuous with colicky exacerbations relieved somewhat by bending forward and drawing up the thighs. He had been nauseated but had

not vomited. He had had similar though less severe pain three weeks and again three days previously which was relieved by passing gas by rectum and which did not cause him to stop work.

He had been followed for eight years in our medical outpatient clinic because of obesity and hypertension. Urine had never been abnormal. When first seen in 1940 his weight was 225 pounds, height 5 feet 7½ inches, and blood pressure 184/116. On his last visit in July, 1947, weight was 205 pounds and blood pressure 170/100. He had been drinking heavily recently and for six months said that he had averaged one to two pints of whiskey daily. Past history was otherwise normal. Two siblings had diabetes. Both parents had died of heart trouble and dropsy, one at 40 years of age and the other at 61. Three siblings had heart trouble.

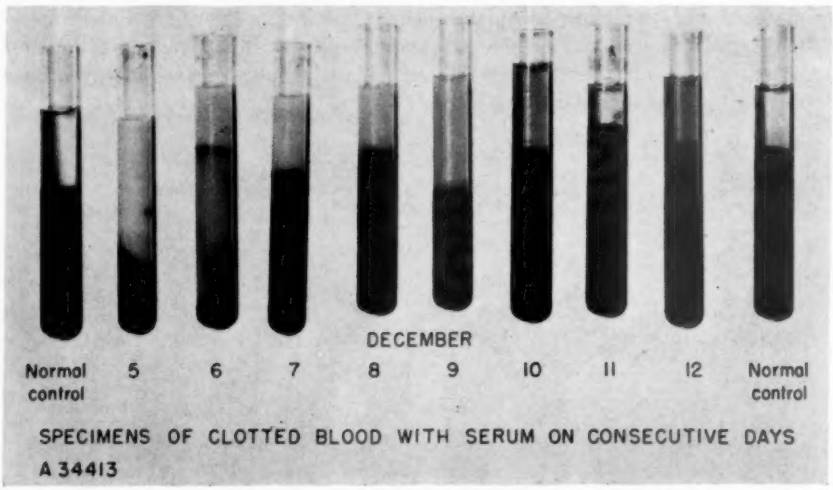

Fig. 2.—(Case 2).—Appearance of blood samples taken from patient in consecutive days. The serum was milky during the first six days.

On examination he was obese, appeared acutely ill, was perspiring freely, and complained bitterly of abdominal pain. He preferred to lie with the thighs flexed. The temperature was 37.2° C., pulse was 100, respirations were 20, and blood pressure was 212/110. The abdomen showed marked tenderness, rebound tenderness, and increase in muscle tone maximum in the epigastrium and right upper quadrant. The left upper quadrant was tympanitic, and the right upper quadrant was dull to percussion. No peristalsis was audible. The remainder of the physical examination showed no significant abnormalities except for moderate arteriosclerotic retinopathy.

Lipemic serum was recognized almost immediately when blood was drawn for chemical test and the serum noted to be milky when clotting occurred. The serum amylase was four plus. The hemoglobin was 14.6 Gm. per cent, white blood count 10,200, urine pH 6.0, specific gravity 1.025, albumin 3 plus, sugar 3 plus, acetone 2 plus. The sediment contained a few granular casts. Blood chemistry determinations showed sugar 250 mg. per cent, CO_2 combining power 50 mg. per cent, nonprotein nitrogen 34 mg. per cent, total cholesterol 1,080 mg. per cent, lipase 0.62 c.c. N/20 Na OH (Normal 0 to 1.5 c.c.), serum neutral fat and fatty acids 7.7 Gm. per cent, serum phospholipids 1,175 mg. per cent, calcium 6.6 mg. per cent, phosphorus 2.4 mg. per cent, alkaline phosphatase 2.6 Bodansky units.

A diagnosis of acute pancreatitis with hyperglycemia and hyperlipemia was made. He was put on constant stomach suction drainage, given a low thoracic paravertebral procaine injection, and intravenous infusions to maintain fluid and electrolyte balance. Within eight hours of admission temperature rose to 39.5° C. (103.2° F.), and then gradually returned to normal in eight days. He developed more severe signs of generalized peritoneal irritation and on the second day he showed signs of circulatory collapse. Blood pressure had dropped from

212/110 on admission to 90/60, the pulse was 150, and he was cold and clammy. The hematocrit was 24. He was given transfusions and the blood pressure was fairly well stabilized around 150 systolic after the second day. During the first twenty-four hours 175 units of regular insulin were given. Thereafter the insulin requirement gradually decreased, until the twelfth day when he was able to take nourishment by mouth and the insulin requirement had stabilized at 35 units of protamine insulin daily. He received 10 c.c. of calcium gluconate and 10 c.c. calcium chloride intravenously daily for ten days, at which time the blood calcium was 8.2 mg. per cent.

The hyperlipemia gradually disappeared (Fig. 2), and the blood serum was clear on the eighth day. The blood cholesterol on this day was 260. The lipase had risen from a normal level on admission to 5.58 c.c. N/20 Na OH (Normal 0 to 1.5 c.c.) on the eighth day. The blood amylase was normal after the fourth day.

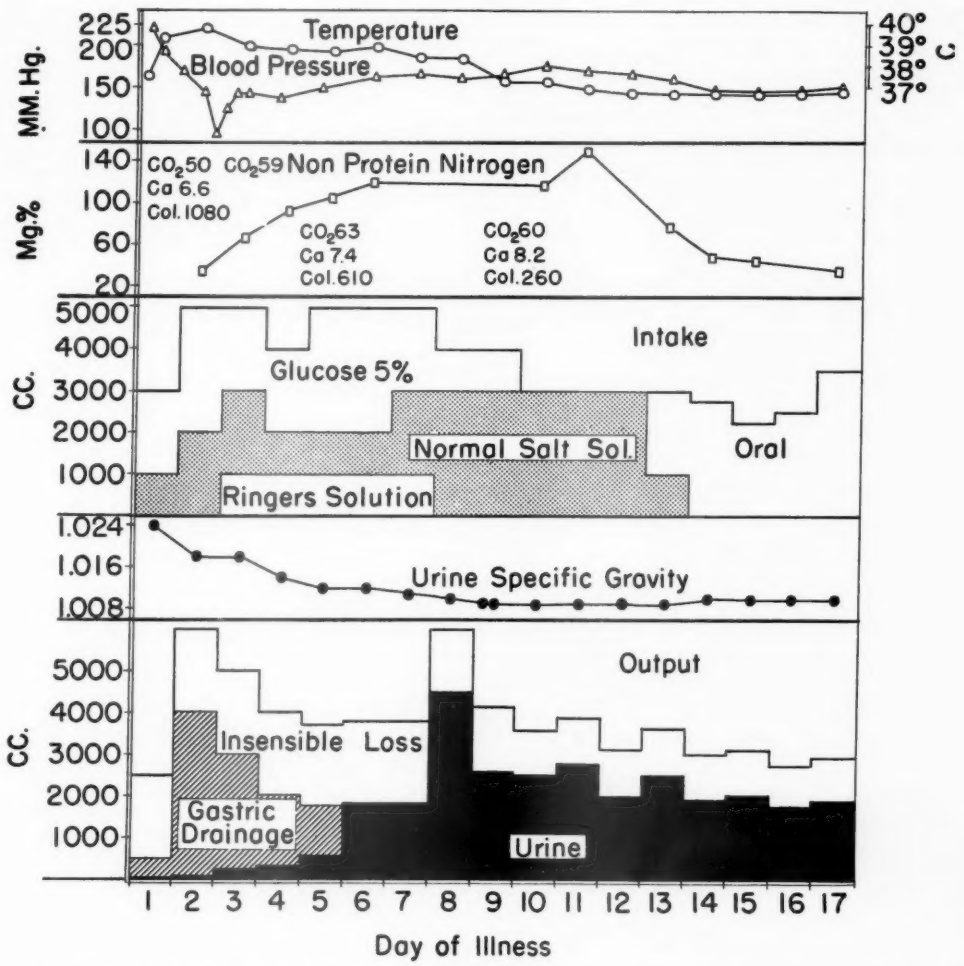

Chart I.—Fluid intake and output, urine specific gravity, and nonprotein nitrogen. Chart in Case 2 showing the progress of the kidney lesion.

Urinary output (Chart I) was suppressed during the first four days when it varied between 90 to 260 c.c. daily and showed a specific gravity 1.012 to 1.018. The nonprotein nitrogen gradually rose to a high of 150 mg. per cent on the tenth day. This occurred in spite of a mounting urinary output to a level of 4,530 c.c. on the ninth day. Urine excreted after the fourth day had a fixed specific gravity level between 1.007 and 1.011. The urine con-

tained no albumin after the twelfth day; however, the centrifuged sediment still contained a few granular casts on discharge. We believe that these findings indicate a lower nephron nephrosis.

Treatment of the kidney injury followed the principles laid down by Coller, Campbell, and Iob,[1] and by Muirhead and Hill,[2] and included (Chart I) transfusion during the phase of hypotension, fluids only in amounts lost in gastric drainage and through skin and lungs during the phase of oliguria, and replacement of fluid and salt lost in the urine during the stage of diuresis.

He was discharged on the eighteenth day of his illness on a diet of protein 80 Gm., fat 90 Gm., carbohydrate 170 Gm., taking 35 units of protamine insulin daily. Gall bladder x-rays on the day before discharge showed no dye in the gall bladder.

He has been followed regularly in the outpatient clinic, and has remained free of pain. Gall bladder x-ray pictures made two months after the acute attack showed the gall bladder to fill and to empty fairly well after the fat meal. He continues to have a mild diabetes well controlled by diet and 25 units of protamine insulin daily. The Mosenthal test showed normal concentration of urine six weeks following discharge from the hospital.

Four weeks after onset of symptoms the total serum lipids were 1,062 mg. per cent, lipid phosphorous 6.7 mg. per cent, phospholipids 167 mg. per cent, total cholesterol 260 mg. per cent, and serum neutral fats and free fatty acids 635 mg. per cent. All of these findings were on the upper limits of normal. After three months the total cholesterol had dropped to 160 mg. per cent.

DISCUSSION

The surgical literature on pancreatitis makes no mention of elevation of blood fats. Thannhauser[3] in his monograph on the lipoidoses, however, quoted Wijnhausen,[4] Marchand,[5] Joel,[6] Brunner,[7] Bernhard,[8] and Marcus[9] as having described hyperlipemia occurring with pancreatitis, and he classified pancreatitis as being one of the five causes of hyperlipemia.*

Root,[10] in 1937, in an analysis of twenty-six patients who died during diabetic coma, found four with acute pancreatitis unsuspected during life. In one of these hyperlipemia had been a constant finding during the terminal illness. This case is similar to the one reported by Marchand.[5] Root also described a fifth patient who survived an attack of acute abdominal pain with hyperlipemia and hyperglycemia in whom a presumptive diagnosis of pancreatitis had been made.

Although idiopathic hyperlipemia with hepatosplenomegaly and secondary xanthomatoses is not the subject of this report it is noteworthy that colicky abdominal pain has been described in three of the six cases (Cases 11 to 17) collected by Thannhauser and in a seventh case reported by Hopgood[18] in 1948. Exploratory laparotomy was done in one case[14] during an attack of pain, but the condition of the pancreas was not observed. Autopsy on another of the patients[16] who had never had abdominal pain disclosed no gross or microscopic abnormality in the pancreas. All except the last of these cases occurred in children. None had disturbances in carbohydrate metabolism. Holt[14] observed in his case that the abdominal pain occurred when the blood fat exceeded a critical level of 8 per cent, that the blood fats dropped abruptly

*Thannhauser's classification of hyperlipemia is as follows: A. Idiopathic hyperlipemia with hepatosplenomegaly and secondary xanthomata. B. Diabetic hyperlipemia. C. Hyperlipemia with pancreatitis. D. Hyperlipemia in glycogen storage disease. E. Hyperlipemia in lipoid nephrosis.

on the first day of the attack, and that the liver and spleen were found greatly increased in size as soon as the abdominal rigidity which accompanied the pain subsided enough to allow abdominal examination. He concluded that the fat removed from the blood went to the liver and spleen and that its accumulation there caused pain from distention of the capsule of these organs.

Collett and Kennedy[19] in 1948 reported on an 8-year-old child with many of the features of idiopathic hyperlipemia, who had had three previous laparotomies for a ruptured abscess of the pancreas with peritonitis. The child had chylous blood serum when studied during a pain-free interval. When he was seen later during an attack of pain, the blood fats were not as high as on the original observation. These authors classified their patient as falling into the group with hyperlipemia and pancreatitis. The child had had glycosuria on one occasion, but had a flat glucose tolerance curve when studied.

The occasional occurrence of hyperglycemia and glycosuria with acute pancreatitis is generally recognized. Schumacker[20] in an analysis of the literature in 1940 noted glycosuria in 11 per cent of patients with acute pancreatitis. He stated that 2 per cent of all patients with severe pancreatitis develop diabetes immediately and that 3 to 10 per cent of those who survive will develop it in time.

Since hyperlipemia is recognized as occurring occasionally in patients with severe diabetes the question arises as to whether the hyperlipemia of pancreatitis is merely a complication of an associated diabetes or whether it can occur from pancreatic injury without a disturbance in carbohydrate metabolism. In the four cases reported by Marcus,[9] the two by Joel,[6] and one by Bernhard[8] hyperlipemia with pancreatitis occurred without diabetes. Thannhauser in reviewing these cases concluded that although the diabetes and the hyperlipemia which may complicate pancreatitis occur as a result of damage to the same organ, the respective conditions are produced by distinctly different functions of this organ. One is the antidiabetic and the other the antilipemic function, either one of which, he believes, may be affected alone. Dragstedt[21] in 1936 isolated a hormone (lipocaic) from extracts of beef pancreas which prevented and relieved fatty degeneration and infiltration of the liver in depancreatized dogs. It is the suppression of such a hormone which may be the cause of hyperlipemia in patients with pancreatitis.

Wijnhausen[4] and Brunner[7] each reported a case of transient hyperlipemia with glycosuria and acute pancreatitis similar to ours. In both of our cases the hyperlipemia was transient and was associated with a high blood sugar and ketonuria, but without more than a very mild acidosis. In both, the hyperlipemia disappeared as the attack subsided and carbohydrate metabolism approximated normal. One patient was known to have had sugar in the urine eighteen months before we saw him. He developed an eruptive form of xanthomatosis at the onset of the present attack, which has now completely disappeared. The other patient had been followed for eight years in our clinic because of hypertension prior to the present illness and had never had sugar in the urine. Both were obese. The second patient had used alcohol excessively prior to the onset of the attack. It is impossible to state whether the

hyperlipemia which occurred in these two patients was caused by suppression of an antilipemic hormone from direct damage to the pancreas or whether it was secondary to diabetes. Since Joslin[22] reported transient lipemia in diabetic patients only when coma or acidosis is also present, it would seem to us, since neither of our patients were in acidosis, that the condition we describe is not a complication of diabetes, but the result of suppression of an antilipemic factor resulting from pancreatic injury.

Large doses of insulin were effective in both of our patients in relieving the hyperglycemia and the hyperlipemia. Constant stomach suction drainage, maintenance of fluid, salt, and calcium balance, and transfusion constituted the other factors in therapy which resulted in complete subsidence of all signs and symptoms except for the continuance of a mild form of diabetes in both patients.

These two cases suggest the need to investigate the possible presence of damage to both pancreatic hormonal factors (antidiabetic and antilipemic) in patients with acute pancreatitis.

SUMMARY AND CONCLUSIONS

Two patients with acute pancreatitis, transient hyperlipemia, and hyperglycemia are described. Both survived under a conservative regime which included large doses of insulin, constant suction drainage of the stomach, transfusions, and maintenance of fluid and electrolyte balance.

Both patients developed high blood sugars with the hyperlipemia. In both, the hyperlipemia disappeared as the attack subsided and carbohydrate metabolism was brought under control with insulin. Neither patient was recognized as diabetic before his attack, though both are considered to be mildly diabetic now. Their hyperlipemia is considered to be the direct result of pancreatic injury on fat and carbohydrate metabolism rather than the result of diabetes alone.

The need to investigate possible damage to both antidiabetic and antilipemic hormonal factors in patients with pancreatitis is urged. A disturbed carbohydrate and fat metabolism if left uncorrected may of itself be a cause of death in patients with pancreatitis.

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MORBIDITY AND MORTALITY IN RUPTURED LIVER

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INTRODUCTION

THE purpose of this paper is to correlate the morbidity and mortality rate of traumatic rupture of the liver before and after the introduction of absorbable hemostatics such as Gelfoam and Oxycel.

Forty cases of patients with ruptured liver admitted to the Boston City Hospital between the years of 1935 to 1945, inclusive, were reviewed. Only those cases with subcutaneous or nonpenetrating liver injuries were considered for this report. Approximately ten patients with ruptured liver are admitted to the surgical services of the Boston City Hospital each year. Though this figure may seem low, it is relatively high, due to the fact that many large hospitals admit only one or two such patients a year.

CAUSE OF RUPTURED LIVER

Hepatic trauma resulted from crushing injuries to the abdomen in 2 cases: one, where a person was crushed in an elevator shaft, and another where a truck backed up and pinned a person against a wall. A fall from a height, as from a railroad bridge or a second story window, accounted for 6 cases. Most of these were due to suicide attempts. A fall from a small height such as down a few stairs was responsible for 2 cases of hepatic injury. Coasting accidents and direct assault as in a fist fight accounted for 3 cases of ruptured liver. Approximately two-thirds (26 cases) of all the ruptured livers were due to some form of automobile violence or collision. It is interesting to note that in coasting accidents where ruptured spleen commonly occurred, ruptured liver occurred infrequently.

SEX

There were 32 males with ruptured liver as compared to 8 females, a ratio of 4:1.

AGE

Most of the patients with ruptured liver were in the second, third, and fourth decades of life. Three cases occurred in the 1 to 10 year age group; 9 cases in the 10 to 20 age group; 6 cases each in the 20 to 30 and 30 to 40 age groups; 3 cases in the 40 to 50 age group; 5 cases in the 50 to 60 age group; and 1 case each in the 60 to 70 and 70 to 80 age groups.

MORTALITY

The total mortality for subcutaneous injured livers, regardless of the type of treatment used, was 62.5 per cent (25 cases). The mortality for nonoperative cases was 81.8 per cent (18 cases). The operative mortality, on the other hand, was 38.9 per cent (7 cases). When chemotherapy in the form of sulfonamide drugs was used, the mortality dropped to 33⅓ per cent (6 cases). Glancing at these figures it is evident that the mortality rate in ruptured livers is very high. Boljarski's[1] mortality rate for subcutaneous liver injuries was 88 per cent, while Thöle[2] found the operative mortality in subcutaneous and percutaneous ruptured livers to be 39 per cent. Madding[3] re-

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ported a mortality rate of 27 per cent in 829 patients with liver injuries in World War II regardless of the type of treatment used. Our figures coincide with those of Thöle, while Boljarski's figures appear to be too high and those of Madding are not representative.

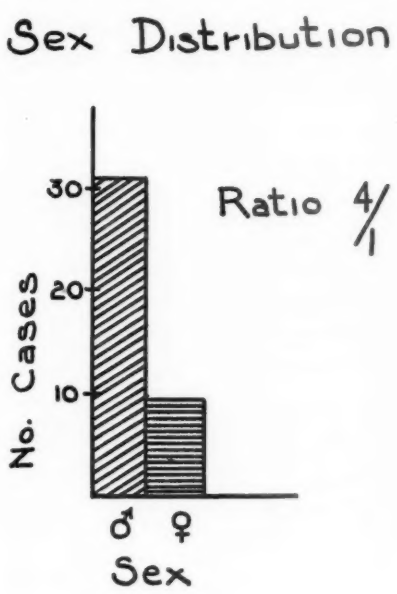
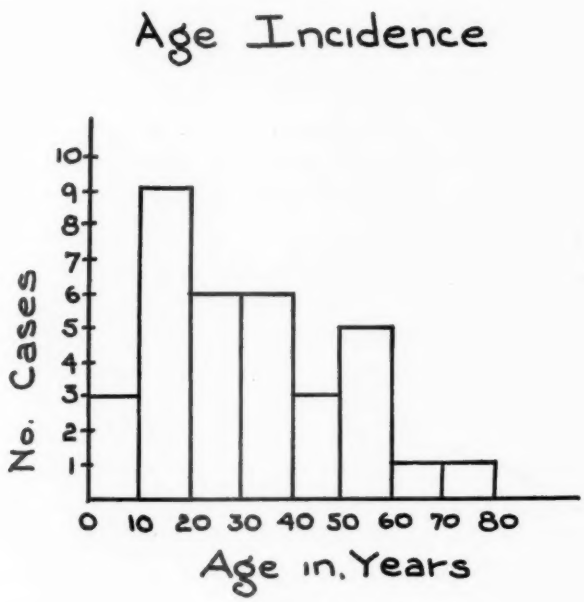


Fig. 1.



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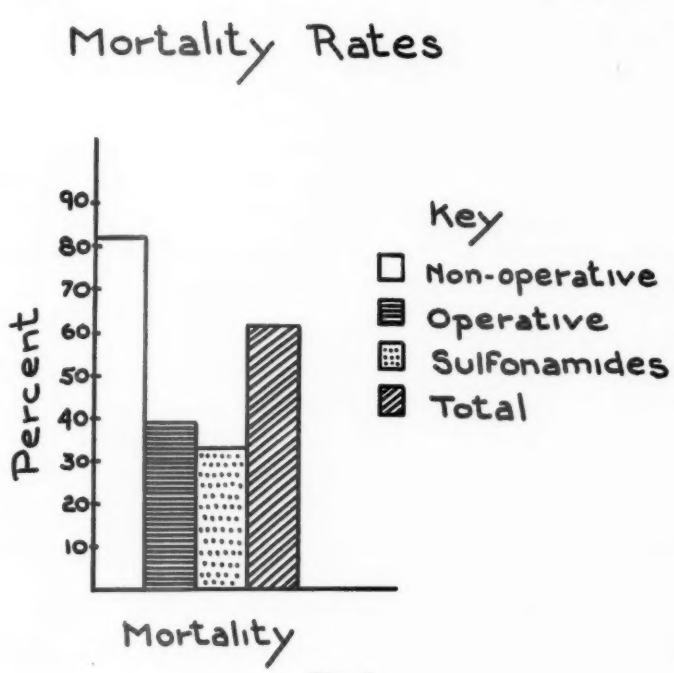

Fig. 3.

EARLY OPERATION VERSUS DELAYED OPERATION

Surgery, when performed within the first three hours after hospital admission, was associated with a mortality rate of 33⅓ per cent. After three hours, the mortality rate rose to 66 per cent. After twelve hours, the operative mor-

tality dropped to zero. Despite the fact that all patients appeared to be out of shock when operated upon, the mortality was greater when surgery was performed from three to twelve hours after admission. Thöle found an operative mortality of 39 per cent in penetrating and subcutaneous injuries of the liver the first six hours after injury; 50 per cent, six to twelve hours after injury; and 67 per cent, twelve to twenty-four hours after injury. This last figure of 67 per cent may be high due to the fact that indirect transfusions of whole blood and plasma were not available in Thöle's time. Our figures indicate the value of early operation within the first three hours after liver injury and a critical period of operability between three to twelve hours after injury.

Some of the reasons why the operative mortality was zero when operation was performed after twelve hours after injury are: (1) adequate transfusions to combat shock; (2) smaller size of liver lacerations; and (3) ability of patient to control the hepatic bleeding by adequate clot formation. The latter two factors must play some part in postoperative recovery, because all patients in this series who were operated upon were adequately treated for shock and appeared clinically to be out of shock at the time of operation. Death from ruptured livers usually occurs within a few hours after injury and is due to hemorrhagic shock from the extensive liver lacerations. The hemorrhage in these cases cannot be controlled by the patient or by transfusions of whole blood. It must be checked by operative methods which control hepatic bleeding and should be accompanied by adequate transfusions. It is evident that early operation and transfusions to combat shock are essential features in the treatment of severely lacerated livers.

SITE OF LIVER LACERATION

The right lobe of the liver was lacerated 4.67 times more frequently than the left lobe of the liver (14 cases to 3). The superior and inferior surfaces of the livers were lacerated with equal frequency (8 cases each). In one case, the caudate lobe was torn. Most of the patients who died soon after admission showed diffusely lacerated livers on autopsy.

ASSOCIATED VISCERAL AND BODILY INJURIES

Either operatively or by autopsy, the kidneys were found injured in 20 per cent of the cases. The spleen was injured in 10 per cent of the cases, and the lungs in 17.5 per cent. The aorta was ruptured in 1 case and the diaphragm ruptured in 2 cases. Ribs were broken in 37.5 per cent patients, and other bones were fractured in over 50 per cent of the cases. Thus, it is evident that patients with ruptured liver commonly have other visceral and bony injuries.

OPERATION BEFORE USE OF HEMOSTATIC AGENTS

All operations were performed under spinal or gas-oxygen-ether anesthesia. Spinal anesthesia was used chiefly in adults and gas-oxygen-ether in children. Of the 18 patients with ruptured liver treated surgically, 15 had a right rectus splitting incision, and 2 had an upper transverse or oblique incision. A right paraumbilical incision was used in one patient in which the diagnosis of ruptured liver was obscured.

The operative treatment consisted of sucking out all of the blood from the peritoneal cavity and either packing the liver laceration with gauze (14 cases), suturing the lacerated liver with chromic catgut (1 case), or packing the laceration in the liver with muscle (1 case). The gauze packing was either

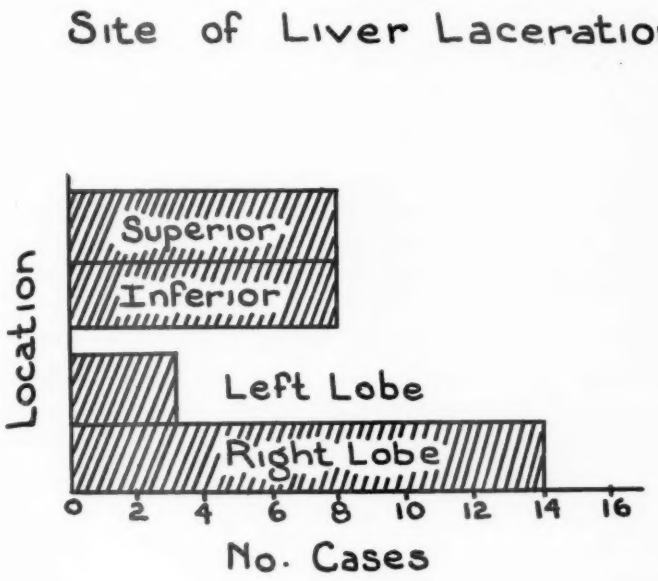

Fig. 4.

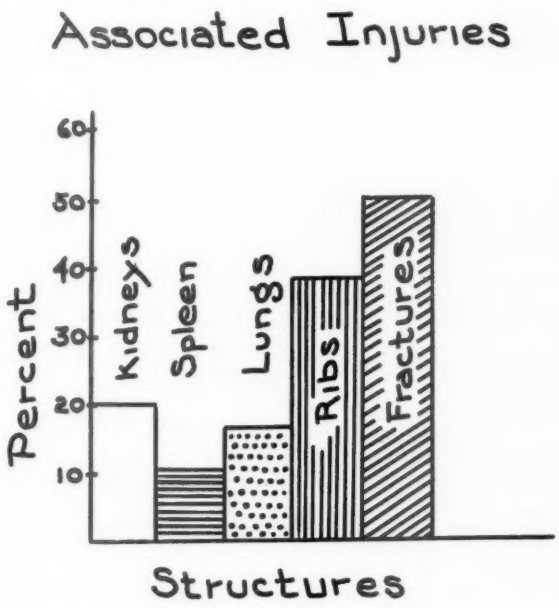

Fig. 5.

brought out through the abdominal incision (8 cases), or through a separate stab wound (3 cases). In 2 cases Penrose drains were inserted into the liver laceration and brought out through the abdominal incision. The peritoneal cavity was drained in all instances.

POSTOPERATIVE CARE

Most of the patients were treated with intragastric suction for three to thirteen days postoperatively. The gauze strips packed into the liver laceration were removed usually under ether anesthesia from the second to the seventeenth postoperative days. Penrose and cigarette drains were removed on the eighth or ninth postoperative days. Ambulation was allowed on the twenty-third to the thirtieth days. One patient was not ambulatory for sixty-eight days and another for seventy-three days. All of these cases occurred prior to the period of early ambulation and only one patient died of pulmonary embolism. Spiking temperatures occurred in all patients and lasted ten to seventy days with the average being thirty days. The length of hospital stay varied from 21 to 100 days, with the average being one month. From these data it is noted that patients with ruptured liver run a stormy course and have a prolonged hospital stay.

COMPLICATIONS

Postoperative complications consisted of biliary fistula, hemothorax, pneumonia, abdominal wall abscesses, subphrenic abscess, septicemia, ventral hernia, and pulmonary embolism. Biliary fistulas occurred in 5 cases after removal of the liver packs. Subphrenic abscesses developed in 3 of the patients between the eighteenth and thirty-ninth days. Thoracotomy with rib resection was required in 2 of these cases. Abdominal wall abscesses occurred in 6 patients, while pneumonia developed in 3, and hemothorax in 2.

CAUSE OF DEATH

The most common cause of death was shock from hemorrhage which occurred in over 80 per cent of the admission mortalities. Of the 16 nonoperative deaths, 10 patients died within the first hour after hospital admission, while 4 more died three hours after hospital admission. All of these patients died of shock. Of the 7 deaths occurring in the operative cases, 1 patient died five minutes after operation from shock, while 2 died from shock the first postoperative day, and 1 from pulmonary embolism. One patient died in shock on the fourth postoperative day from delayed liver hemorrhage. Another operative patient died the sixth postoperative day from renal failure due to thrombosis of the right renal artery, while another died on the thirteenth postoperative day from biliary peritonitis. Thus, hemorrhagic shock was the most common cause of death in both operative and nonoperative patients; whereas delayed liver hemorrhage, renal failure, and biliary peritonitis were other causes of operative deaths.

OPERATION AFTER THE USE OF HEMOSTATIC AGENTS

Subcutaneous rupture of the liver is associated with a high mortality rate. In this series of 40 cases, the over-all mortality rate was 62.5 per cent, and the operative mortality rate before the use of absorbable hemostatic agents was 38.9 per cent.

In an attempt to lower the prohibitive mortality and morbidity in this condition we sought for new operative criteria and techniques. It has been shown in animals with ruptured livers that recovery can be enhanced by con-

trolling hepatic hemorrhage with absorbable hemostatic packs.[4, 5, 6] It has also been observed, that in cases of human ruptured liver, whenever the abdomen was drained, postoperative complications such as subphrenic abscess, biliary fistula, abdominal wall abscess, and ventral hernia frequently developed. Hence, the technique put forth by us in treating ruptured livers consisted of: (1) administering whole blood for shock; (2) performing early operation; (3) packing the liver laceration with absorbable hemostatic sponges; and (4) closing the abdomen without drainage.[7]

With the use of this technique in 3 cases of ruptured liver at the Boston City Hospital within the past year, all patients recovered without postoperative complication. In one other patient treated similarly except for abdominal drainage, a subphrenic abscess developed which required thoracotomy.

Some of the methods used in treating the liver laceration were: (1) simple packing of the laceration with absorbable hemostatic sponges; (2) suture of the absorbable Gelfoam or Oxycel sponges to the liver capsule; (3) simple packing of the liver laceration with Oxycel or Gelfoam, combined with suture of the liver capsule to the diaphragm to prevent the suction effect of the diaphragm on the liver.

The operative mortality in the last 4 patients with ruptured liver at the Boston City Hospital treated with the technique outlined here was zero.

SUMMARY

1. The total mortality rate for subcutaneous ruptured livers at the Boston City Hospital between the period of 1935 to 1945 was 62.5 per cent regardless of the type of treatment used.

2. The operative mortality for subcutaneous ruptured livers using gauze, muscle, or catgut sutures to control the hepatic hemorrhage was 38.9 per cent.

3. The operative mortality rate dropped to 33⅓ per cent when sulfonamides were used.

4. In the last 4 patients with ruptured liver treated surgically at the Boston City Hospital using the criteria of treating shock and performing early operation with control of hepatic hemorrhage by using Oxycel or Gelfoam packs, the operative mortality was reduced to zero.

5. The morbidity in ruptured liver is lowered by abdominal closure without drainage.

6. The most frequent cause of immediate death in ruptured livers is shock.

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THE EFFECT OF VAGOTOMY AND ANTRUM RESECTION ON THE MANN-WILLIAMSON ULCER

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SURGICAL internal duodenal drainage in the dog as described by Mann and Williamson[1] regularly produces chronic peptic ulceration at the gastrojejunal stoma. This discovery has proved to be of great importance in the study of the pathogenesis of these lesions, and it has also made possible an evaluation of various therapeutic procedures both as prophylactic and as curative measures under the controlled conditions of the laboratory. It seems probable that the explanation proposed for the cause of these ulcers is correct, namely, that they are due to the corrosive effect of the acid gastric content on the jejunal mucosa when deprived of the continuous neutralizing effect of the alkaline duodenal secretions. Gastric secretion in these animals is probably normal, since neither the neurogenic nor the humoral mechanism for stimulating secretion is interfered with. The buffer mechanism supplied by swallowed food and saliva and gastric mucus is still present, but is ineffective in protecting the mucosa in the absence of the alkaline secretions from the pancreas, liver, and duodenum.

Section of the vagus nerves to the stomach decreases the acid output by eliminating the cephalic phase of gastric secretion, and this procedure has been found effective in the treatment of duodenal and gastrojejunal ulcers in man. The antrum of the stomach has long been thought to play an important role in gastric secretion, largely on the basis of indirect evidence. In a series of studies recently reported from this laboratory,[2] quantitative data have been secured following antrum resection in Pavlov pouch dogs which prove conclusively that complete removal of the antrum decreases the secretion of gastric juice from a Pavlov pouch by from 60 to 90 per cent. While there is now considerable doubt that the Pavlov pouch accurately reflects the secretory activity of the entire stomach, these data indicate the special importance of the antrum in the gastric phase of secretion. Resection of the antrum of the stomach was for a long time practiced in the treatment of duodenal ulcer, and favorable results were secured in many cases. It was the purpose of the present investigation to determine if vagus section, antrum resection, or a combination of both procedures will decrease acid production sufficiently to delay or to prevent formation of Mann-Williamson ulcers.

Beaver and Mann in 1931[3] reported that two out of three vagotomized Mann-Williamson dogs developed ulcers. All five dogs in Oliver's series[4] with vagus section, plus the Mann-Williamson procedure, developed ulcers. Saltzstein and his associates[5] found ulcers in four out of twelve such dogs, but many

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succumbed prematurely to nutritional deficiencies. However, only one out of nine in Harkins' series[6] of Mann-Williamson animals with vagotomy developed ulcers. In a series of seventeen dogs in which the Mann-Williamson procedure plus vagotomy was carried out by Enerson, Woodward, Tovee, Neal, Sibley, and Dragstedt,[7] only six, or 35 per cent, developed chronic ulcers. Recently, Oliver[8] has investigated the effect of subtotal gastrectomy with and without vagus section on the course of the Mann-Williamson dog. All of four dogs with subtotal gastrectomy, plus the Mann-Williamson procedure, developed ulcers, but none of six animals with vagus section, three-quarter gastrectomy, and the Mann-Williamson procedure developed ulcers. All six of the latter group had severe nutritional failure.

EXPERIMENTAL PROCEDURE

In a control series of nine normal dogs, the standard Mann-Williamson procedure was carried out. The pylorus was transected and the duodenal stump closed. The jejunum was then transected about 10 cm. beyond the ligament of Treitz and the proximal end implanted end to side into the ileum about 30 cm. proximal to the cecum. Continuity of the gastrointestinal tract was re-established by anastomosing the pyloric portion of the stomach to the distal segment of jejunum by an end-to-side anastomosis. In the second series of eleven dogs, bilateral division of the vagus nerves was first performed by the transthoracic approach under positive-pressure ether anesthesia. Four to six weeks later, the Mann-Williamson procedure was done. In Series 3, consisting of six animals, the gastric antrum, comprising about one-fourth of the stomach, was resected, and the fundus anastomosed to the distal segment of jejunum in completing the Mann-Williamson procedure. An identical procedure was used in Series 4 after a preceding division of the vagus nerves carried out as in Series 2. All of the animals were given intravenous Ringer's solution and penicillin for three days postoperatively and were then fed the stock diet of the laboratory.

The results obtained are shown in Tables I to IV and are summarized in Table V.

TABLE I. SERIES 1. MANN-WILLIAMSON CONTROL SERIES

DOG NO.	ULCER PRESENT	SURVIVAL TIME (DAYS)	REMARKS
D-885	+	52	Perforated ulcer
D-896	+	37	Perforated ulcer
D-903	+	22	Perforated ulcer
D-920	+	64	Perforated ulcer
D-911	+	130	Perforated ulcer
D-929	+	65	Perforated ulcer
D-935	+	68	3 ulcers, no perforation
D-40	+	94	Perforated ulcer
D-53	+	78	Ulcer; died of intussusception
No. of dogs, 9	No. of dogs with ulcers, 9	Avg. survival time (dogs with ulcers), 68	

TABLE II. SERIES 2. MANN-WILLIAMSON PLUS VAGUS SECTION

DOG. NO.	ULCER PRESENT	SURVIVAL TIME (DAYS)	REMARKS
D-849	0	65	
D-855	+	122	Perforated ulcer
D-862	+	105	Perforated ulcer
D-857	+	24	Perforated ulcer
D-867	0	48	
D-880	+	60	Perforated ulcer
D-917	+	52	Perforated ulcer
D-951	0	87	
D-955	0	69	
D-942	0	144	
D-956	0	280	Sacrificed; condition excellent
No. of dogs, 11	No. of dogs with ulcers, 5	Avg. survival time (dogs with ulcers), 73	

TABLE III. SERIES 3. MANN-WILLIAMSON PLUS ANTRUM RESECTION

DOG. NO.	ULCER PRESENT	SURVIVAL TIME (DAYS)	REMARKS
D-997	0	225	Sacrificed; condition excellent
D-999	+	191	Died of hemorrhage from ulcer
D-2	0	214	Sacrificed; condition good
D-8	0	108	Died of intestinal obstruction
D-7	+	145	Perforated ulcer
D-14	0	182	Sacrificed; condition fair
No. of dogs, 6	No. of dogs with ulcers, 2	Avg. survival time (dogs with ulcers), 168	

TABLE IV. SERIES 4. MANN-WILLIAMSON PLUS ANTRUM RESECTION AND VAGUS SECTION

DOG. NO.	ULCER PRESENT	SURVIVAL TIME (DAYS)	REMARKS
D-1000	0	153	Died of inanition
D-4	0	194	Sacrificed; condition excellent
D-23	0	127	Died of inanition
D-30	0	181	Sacrificed; condition poor
D-35	+	153	Died of perforated ulcer
D-37	0	132	Died of inanition
No. of dogs, 6	No. of dogs with ulcers, one	Avg. survival time (dogs with ulcers), 153	

DISCUSSION

All of the nine animals in the control series developed typical Mann-Williamson ulcers with an average survival time of sixty-eight days. In the series with vagus section, about one-half (45 per cent) of the animals developed ulcers with a survival time essentially the same as in the control group. It should be noted that although slightly over one-half of the animals were completely protected from the Mann-Williamson ulcer by vagus section alone,

TABLE V. SUMMARY

	NO. OF DOGS	NO. OF ULCERS	PER CENT OF ULCERS	AVG. SURVIVAL TIME OF DOGS WITH ULCERS (DAYS)
Control Mann-Williamson	9	9	100	68
Mann-Williamson plus vagus section	11	5	45	73
Mann-Williamson plus antrum resection	6	2	33	168
Mann-Williamson plus antrum resection and vagus section	6	1	17	153

those developing the ulcers did so in the same length of time as the controls. Resection of the gastric antrum afforded complete protection from experimental ulcer to two-thirds of the animals. In the two animals that did develop ulcer, there was a pronounced delay with a survival time two and one-half times that found in the control and in the vagotomized group. Combination of antrum resection and vagus section afforded complete protection to the majority (83 per cent) of the animals. The one animal in this series that developed an ulcer showed the same prolongation of survival time noted with antrum resection alone.

It is quite clear from this study that whereas bilateral vagotomy and antrum resection delay the appearance of Mann-Williamson ulcers, these procedures are by no means so effective in this group of experimental ulcer as they have been found to be in the treatment of duodenal ulcer in man. In the few years since vagotomy was introduced,[9] the opinion of almost all surgeons is apparently unanimous that this procedure is a satisfactory treatment for gastrojejunal ulcer following the performance of either gastroenterostomy or gastric resection. While resection of the antrum alone has been abandoned in the treatment of duodenal ulcer in favor of the more extensive subtotal gastric resection, nevertheless, the incidence of recurrent jejunal ulcer following antrum resection in duodenal ulcer in man was by no means as high as we have found the incidence of Mann-Williamson ulcers to be in dogs with previous antrum resection. What is the explanation for this marked difference in response to vagotomy and to antrum resection displayed by the experimental as compared with the clinical ulcer? Is the Mann-Williamson ulcer in dogs strictly comparable to the stoma ulcer seen in man? These are important, practical, as well as theoretical questions. One obvious difference between the two lesions depends upon the fact that in the experimental ulcer, the duodenal secretions are deviated completely into the lower intestine, while in most stoma ulcers in man these secretions pass over the ulcer area. An exception to this latter statement is the stoma ulcer that develops when a Roux or Y-type of gastroenterostomy is performed. Exalto[10] many years ago called attention to the high incidence of stoma ulcers with this type of anastomosis, both when done for duodenal ulcer in man or when constructed in normal dogs. It is quite likely that the pathogenesis of these experimental ulcers of Exalto is similar to that of the

Mann-Williamson lesion. The Y type of gastroenterostomy has now been abandoned for the treatment of duodenal ulcer, but occasionally stoma ulcers are encountered in man when the situation resembles that in the experimental ulcers of Exalto and of Mann and Williamson. Accordingly, it is unwise to use the Mann-Williamson preparation as a test object for the efficacy of therapeutic measures proposed for peptic ulcers in man. It is much too severe a test. It is probable on the basis of recent findings that most duodenal and stoma ulcers are due to gastric hypersecretion, and that complete absence of the automatic neutralizing effect of the duodenal secretions rarely plays a role in the clinical problem. Gastroenterostomy is not followed by stoma ulcer unless gastric hypersecretion exists, or is experimentally produced, or unless the duodenal secretions are diverted from the area of anastomosis. It is for this reason that jejunal ulcers do not occur after gastroenterostomy in normal dogs, or in man with carcinoma of the stomach, or gastric ulcer associated with normal or depressed secretion.

CONCLUSIONS

1. Removal of the cephalic phase of gastric secretion by division of the vagus nerves protects about one-half of Mann-Williamson dogs from stoma ulcer formation.

2. Removal of the gastric phase of gastric secretion by resection of the gastric antrum protects about two-thirds of Mann-Williamson dogs from stoma ulcer formation. In those developing ulcers, the genesis is markedly delayed.

3. Removal of both cephalic and gastric phases of gastric secretion is more effective than either procedure alone in preventing Mann-Williamson ulcers.

4. There is a significant difference between the Mann-Williamson ulcer in experimental animals and the gastrojejunal ulcer in man following either gastroenterostomy or partial gastrectomy, both in pathogenesis and in response to treatment. The complete deviation of the duodenal secretions from the region of the gastroenterostomy in the Mann-Williamson procedure makes these lesions more intractable and difficult to cure than the usual stoma ulcer in man, where this deviation is not present.

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BLOOD VOLUME IN THE ELDERLY PATIENT BEFORE AND AFTER SURGERY

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DEATH from pulmonary edema and peripheral vasomotor collapse occurs with a disturbing frequency in the elderly patient following surgery. In spite of adequate preparation for surgery and careful replacement therapy over the recovery period there continue to be fatalities. In a large municipal hospital where the majority of the patients are chronically ill, observations were carried out to find the cause of these failures.

Parenteral therapy was based largely on hemoglobin, plasma protein concentration, and urinary output. It included blood, plasma, and fluid replacement as indicated in the judgment of experienced surgeons. It seemed at times that death was a direct result of what was intended to be supportive intravenous therapy. Significant alterations in the blood volume of elderly patients[1, 2] have been known for some time. Apparently vital processes may be stabilized at a lower level of activity with a reduced blood volume. The state of diminished blood volume and circulating plasma protein, weight loss, and increased extracellular fluid in some elderly patients has been described[2, 3] as "chronic shock."

This study attempts to present the problem of reduced blood volume in the elderly chronically ill patient before and after surgery. The extent of blood volume depletion as well as that of total plasma proteins and red cell mass was determined in twelve cases. By repeated readings the patient's clinical course may be better evaluated and specific replacement therapy instituted. It is possible to obtain a greater measure of control over the blood volume which will protect the patient against the improper use of parenteral fluids.

PROCEDURE AND TECHNIQUE

Some of the more important considerations of the cases under study are presented in Table I. The ages of the patients vary from 53 to 79 years. Variations in body weight from the normal are recorded for each particular age and height since the best weight in health was not ascertainable. On this basis two patients show weight over twenty pounds above normal, while five were twenty pounds under normal. Hemodynamic measurements do not indicate disease except in one case of essential hypertension, and one high venous pressure of cardiorespiratory failure. Circulation time of Decholin from arm to tongue is prolonged in six cases above the high normal of eighteen seconds while none was under thirteen. An attempt was made to correlate the surgeon's estimate of the patient's clinical condition with blood volume studies.

The technique in determining plasma volume in this series of cases was a simplified one. It does not involve elaborate or expensive equipment. It consists of a small visual comparator (Hellige) with permanent glass standards.[4] The plasma volume was determined by measuring the difference in color between serum samples taken before and ten minutes after the injection of a

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TABLE I. MEASUREMENTS OF HEIGHT AND WEIGHT, AND HEMODYNAMIC STATUS OF TWELVE PATIENTS IN WHOM DETAILED BLOOD VOLUME STUDIES WERE CARRIED OUT

PATIENT	AGE (YR.)	HT. (IN.)	WT. (LB.)	DEV.* NOR.	B. P.	VEN. P.	PULSE RATE	CIR. TIME	GEN.† CDN.	DIAGNOSIS
1. RA	64	69	160	- 8	160/95	85	84	22	Fa	CNS Syphilis; ventral hernia
2. MB	64	65	156	+ 7	170/88	57	80	13	Gd	Duodenal ulcer
3. RB	59	60	140	+ 7	125/80	47	82	17	Gd	Obstructive jaundice
4. DC	79	66	115	-38	206/100	50	70	18	Fa	Arteriosclerotic gangrene of legs
5. EL	74	62	105	-34	124/64	47	62	22	Pr	Carcinoma of rectum
6. TM	66	62	118	-21	130/60	25	80	23	Fa	Dupuytren's contracture
7. HF	53	57	92	-35	260/115	52	86	23	Fa	Essential hypertension
8. CM	64	64	104	-41	110/70	140	60	20	Pr	Cirrhosis of liver
9. EM	62	66	160	+ 7	112/70	35	84	18	Gd	Inguinal hernia
10. LR	75	64	190	+48	135/60	-	80	-	Fa	Arteriosclerotic gangrene of legs
11. AR	70	62	165	+26	124/80	47	66	23	Gd	Varicose ulcer of leg, chronic
12. SS	63	62	140	+ 1	120/70	30	80	18	Gd	Varicose ulcer of leg, chronic

*Dev. Nor., Weight deviations from normal for that particular height and age.
†Gen. Cdn., This is a clinical estimate of the general physical condition: Gd, good; Fa, fair; Pr, poor.

known amount of the Evans blue dye T-1824[5] after the method described by Noble and Gregersen.[6] They showed that the measurement of a single sample taken ten minutes after injection gives valid results both in normal subjects and in patients in shock. The amount of dye used was 3 c.c. and the blood samples were taken with heparin-coated syringes. It was most essential to obtain nonhemolyzed specimens; otherwise colorimetric readings were difficult to make and more often than not were valueless. No special effort was made to obtain fasting blood samples to obviate any discoloration of plasma from ingestion of fats. The colorimetric readings were checked by each observer and the results obtained were similar in practically all instances.

Red blood cell volumes were calculated from hematocrit values obtained with Sanford-MaGath tubes centrifuged at 2,500 revolutions per minute for fifteen minutes. Hematocrit determinations were doubly checked, once before the dye was injected and again afterward.

Specific gravity of plasma was determined by the copper sulfate method, and plasma protein percentage by the formula of Weech, Reeves, and Goettsch.[7]

Preoperative Blood Volume Studies.—Perhaps no figures reveal the degree of loss of compensatory reserve in the elderly patient so well as those of plasma volume, red cell mass, and plasma proteins (Table II). Plasma volume has been calculated in per cent normal liters per square meter body surface using the 1.94 liters average normal described by Rowntree and Brown.[8] Ten cases vary from a low of 43 to 88 per cent of the normal. The two remaining cases

of 100 and 114 per cent have important reductions in the other blood components which will be described. These low values are considerable and imply a proportionate fall in active vascular space in order to maintain the hemodynamic measurements found in Table I. When the experimental animal is unable to compensate for more than a 40 per cent reduction in blood volume,[9] the compensatory reserve remaining here in these cases must be low indeed.

Too little factual information is available relating to circulating plasma volume in equilibrium with extravascular, lymphatic spaces and plasma protein sources.[10, 11, 12] Although indicating diminished compensatory reserve, reduced plasma volume may not be as significant as a fall in red cell mass or protein concentration.[3, 13, 14]

TABLE II. PREOPERATIVE BLOOD VOLUME STUDIES

PATIENT	HMCT. %	R.B.C. MASS	R.B.C. % N	TOTAL B. VOL. (C.C.)	PL. PR. (GM. %)	TOTAL PL. VOL.	L/M² B.S.*	% N L/M²	DIAGNOSIS
1. RA	41	2220	76	5420	7.2	3200	1.70	87	CNS Syphilis; ventral hernia
2. MB	44	2360	80	5360	6.3	3000	1.70	87	Duodenal ulcer
3. RB	37	1270	50	3425	5.7	2150	1.35	69	Obstructive jaundice
4. DC	50	1900	92	3800	6.3	1900	1.27	63	Arteriosclerotic gangrene of legs
5. EL	29	1300	68	4500	6.3	3200	2.22	114	Carcinoma of rectum
6. TM	40	1730	82	4330	6.1	2600	1.72	87	Dupuytren's contracture
7. HF	40	1334	75	3334	5.5	2000	1.55	80	Essential hypertension
8. CM	33	750	40	2250	5.5	1500	1.02	43	Cirrhosis of liver
9. EM	44	2500	89	5700	6.2	3200	1.77	88	Inguinal hernia
10. LR	51	3122	81	6122	7.2	3000	1.55	80	Arteriosclerotic gangrene of legs
11. AR	45	1850	63	4000	7.4	2150	1.20	62	Varicose ulcer of leg, chronic
12. SS	38	2000	81	5200	6.3	3200	1.96	100	Varicose ulcer of leg, chronic

*L/M² B.S., Liters per square meter of body surface.

A casual plasma protein concentration has proved disappointing. A normal diurnal variation of about 0.80 Gm. per cent occurs in active as well as in inactive subjects.[11, 15] Repeated determinations in the controlled patient have more significance, particularly if consistently low. Only three patients in this series showed relatively normal concentration of 7 Gm. per cent or above, and not one of these had a normal plasma volume. All the others ranged from 6.3 down to 5.5. This, together with the reduction in blood volume, indicates depletion of the sources of plasma protein reserve.

Red cell mass indicates the oxygen-carrying capacity of the blood. To maintain normal hemodynamics the continuous high oxygen requirement of vital organs has to be met. The effect of chronic oxygen lack is well known to impair the adjustment of the circulatory system to changes in blood volume and body position.[16]

All twelve cases present values for circulating red cell mass below 92 per cent of normal and one is less than one-third this value. These are represented by hematocrits varying from 29 to 45 per cent. Note is made of Case 5 with a 29 per cent hematocrit but a plasma volume of 114 per cent. Two patients with a red cell mass over 2,500 c.c. showed reduction in plasma volume although one

had a normal protein concentration. Red cell mass of such low levels hardly can be expected to do more than merely maintain vital organs. A retardation of anabolic processes is understandable.

It is apparent from these data that the desired information on a patient's compensatory reserve is not attainable from hematocrit or plasma protein alone. The clinical impression of the patient's condition does not correlate well with blood studies. Each patient shows an individual need for specific replacement to protect him against injudicious parenteral therapy.

Effect of Rapid Infusion on Plasma Proteins.—Plasma protein determines the effective osmotic pressure of blood and by this means maintains adequate circulating plasma volume. A reduction in protein of 1 Gm. per cent in a patient stabilized at 6.3 Gm. can result in serious loss of plasma volume. Instances of this in postoperative cases are described later (Cases 2 and 5). Parenteral fluid can be shown to have such an effect on plasma protein, as can be seen readily in Table III. The effect can be crucial for inducing pulmonary edema when combined with a rising intravascular pressure, diminished intra-alveolar oxygen, and tissue tension in a lung harassed by stimulating reflexes.[17]

TABLE III. EFFECT OF RAPID INFUSION ON PLASMA PROTEINS

PATIENT	INTRAVENOUS SOLUTION AND RATE	TIME LAPSED* (MIN.)	CHANGE IN PL. PR.	PL. VOL.	BL. VOL.	REMARKS
1. RA	1000 c.c. .9% sal. in 25 min.	30	7.8 → 5.9 -1.9 Gm. %	+600	+674	No change in clinical signs and symptoms
	1000 c.c. .9% sal. in 30 min.	90	7.2 → 6.6 -0.6 Gm. %	+400	+330	No changes
2. MB	1000 c.c. 5% Dex. in H_2O, in 40 min.	50	6.3 → 5.8 -0.5 Gm. %	+200	+254	No changes
3. TM	1000 c.c. 5% Dex. in sal. in 30 min.	60	6.2 → 5.4 -0.8 Gm. %	+300	+600	Pulmonary edema appeared after 800 c.c. were given; it disappeared 10 minutes after completion of infusion

*Time Lapsed. Time interval between the completion of the infusion and the determination of the blood volume.

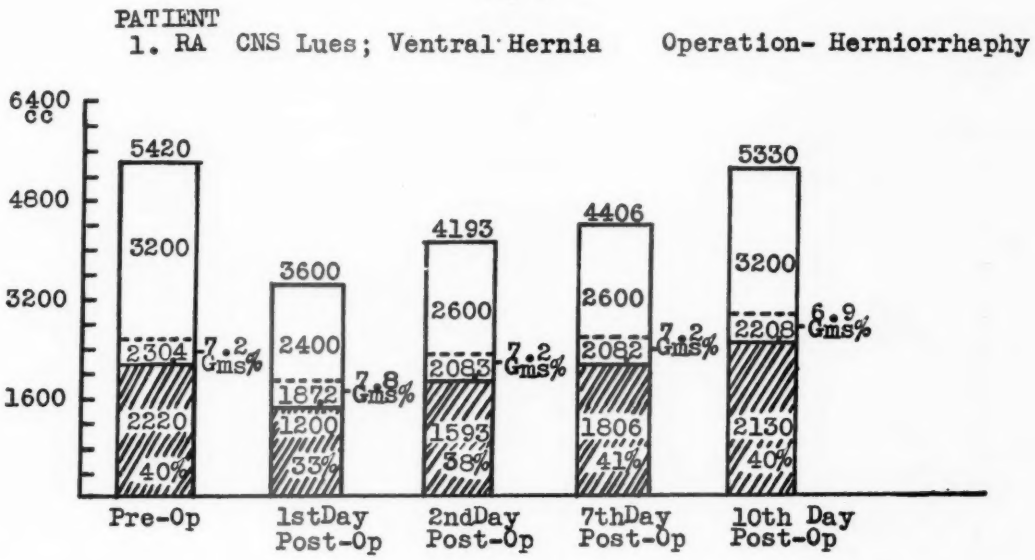
Postoperative Blood Volume.—Six cases are reported in graph form (Figs. 1 to 6). Each shows a different pattern of disturbance following operation and throughout the recovery period. No consistent effect stands out for any given procedure. These data were not used to influence the surgeon's postoperative care of the patient. They were obtained to reveal how inadequately the blood volume was being maintained under the accepted routine management.

CASE 1.—The patient convalesced uneventfully from a large ventral herniorrhaphy. One can see how much strain this simple reparative procedure put on the patient's compensatory reserve.

CASE 2.—There was a failure to correct for a critical loss in plasma protein and plasma volume following an exploratory laparotomy for chronic peptic ulcer. Postoperatively the patient received 1 unit of plasma and seven liters of fluid in fifty hours. Death occurred after the second postoperative day as a result of a drop in total protein and concentration, vasomotor collapse, and anoxia.

CASE 3.—There was a rise in plasma protein concentration following a laparotomy. Red cell mass was relatively undisturbed. However the patient was given 500 c.c. of whole blood on the fourth postoperative day and the rise in red blood cell mass is noted on the graph (Fig. 3).

Fig. 1.



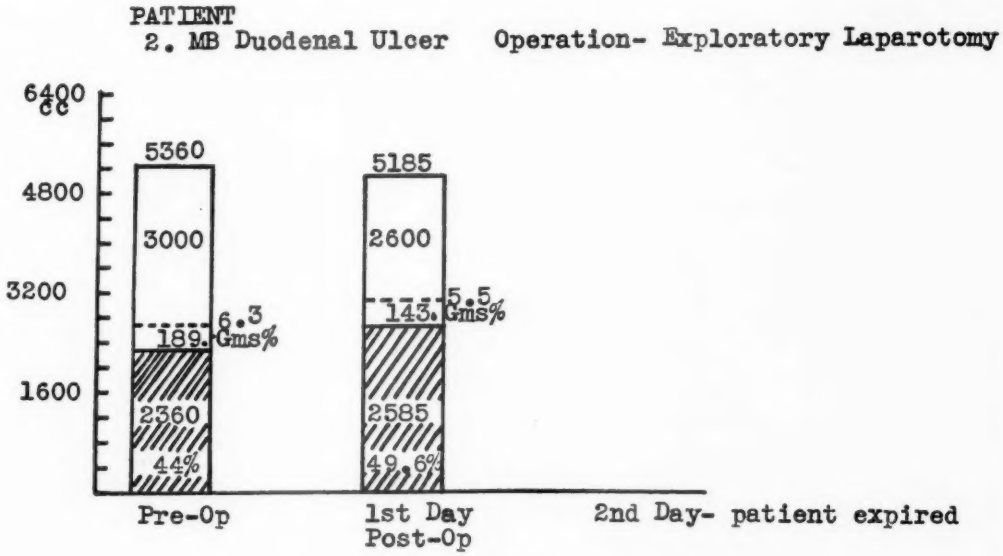


Fig. 2.

CASE 4.—The patient maintained the circulating plasma volume well, but showed a marked fall in red blood cell mass. He received 1,000 c.c. of whole blood and 1,000 c.c. of plasma.

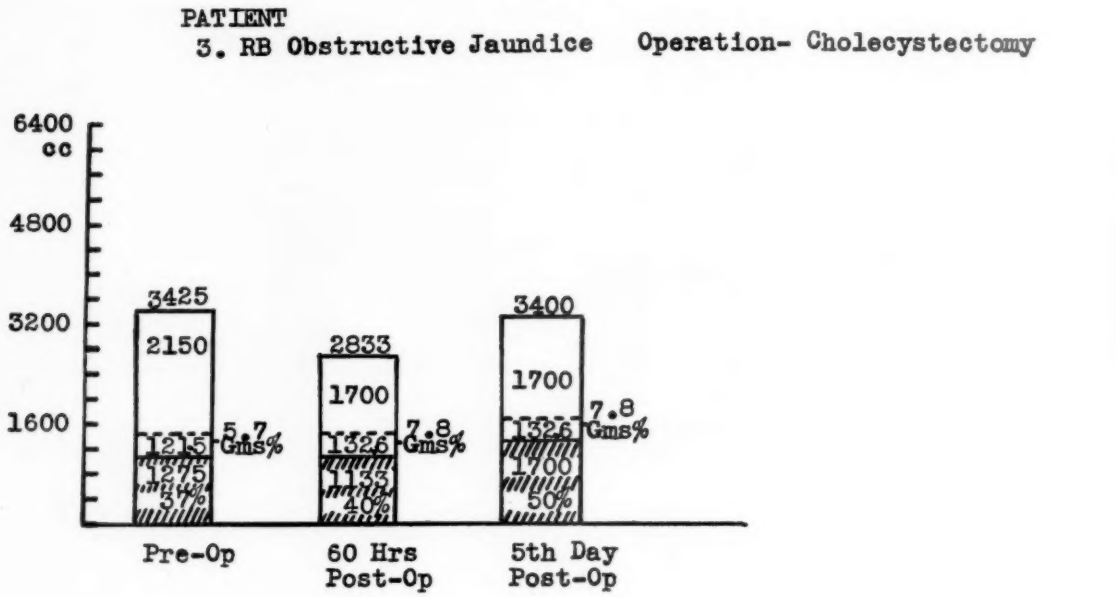
CASE 5.—There was a progressive fall in plasma protein concentration similar to that in Case 2 leading to subminimal maintenance level forty-eight hours prior to death. In spite of whole blood transfusions totaling 3,000 c.c. the compensatory mechanisms could not correct for this added volume. The specific need was for red blood cells and albumin. The vascular space could not handle the additional fluid administered.

CASE 7.—An episode of acute pulmonary edema occurred on the fifth day postoperatively. The edema lasted seven hours and improved with 1 unit of plasma, aminophylline, and positive pressure oxygen breathing. Twelve hours later blood volume showed 40 per cent reduction of red cell mass with increased concentration of plasma proteins.

DISCUSSION

The surgeon cannot be too well aware of the changes occurring in blood volume recorded here for the elderly patient. Oftentimes this makes the dif-

Fig. 3.



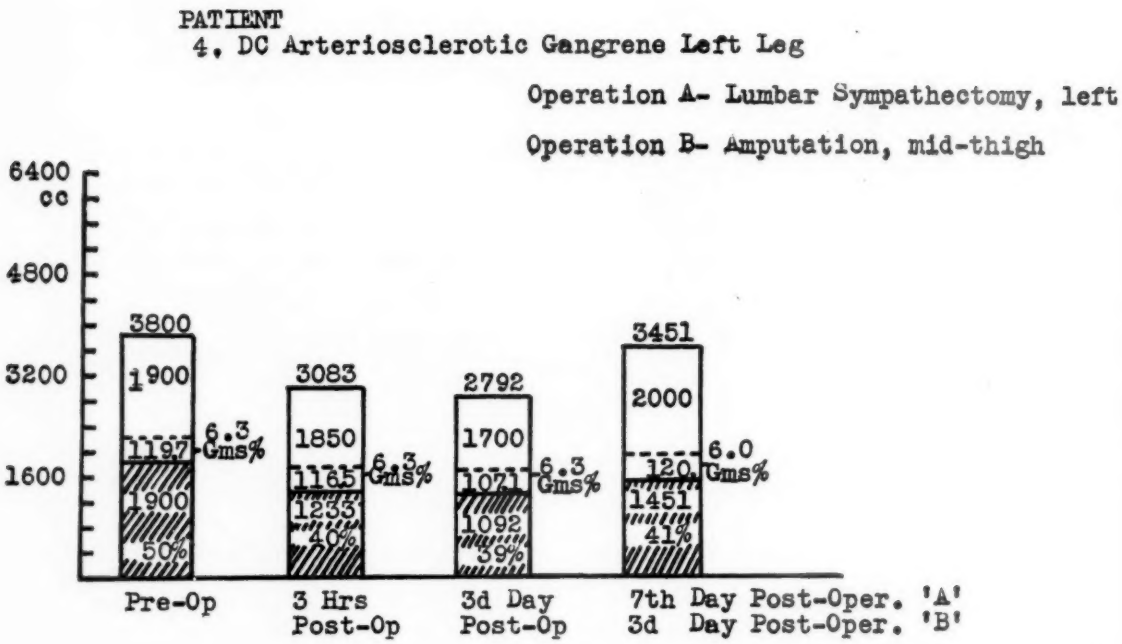
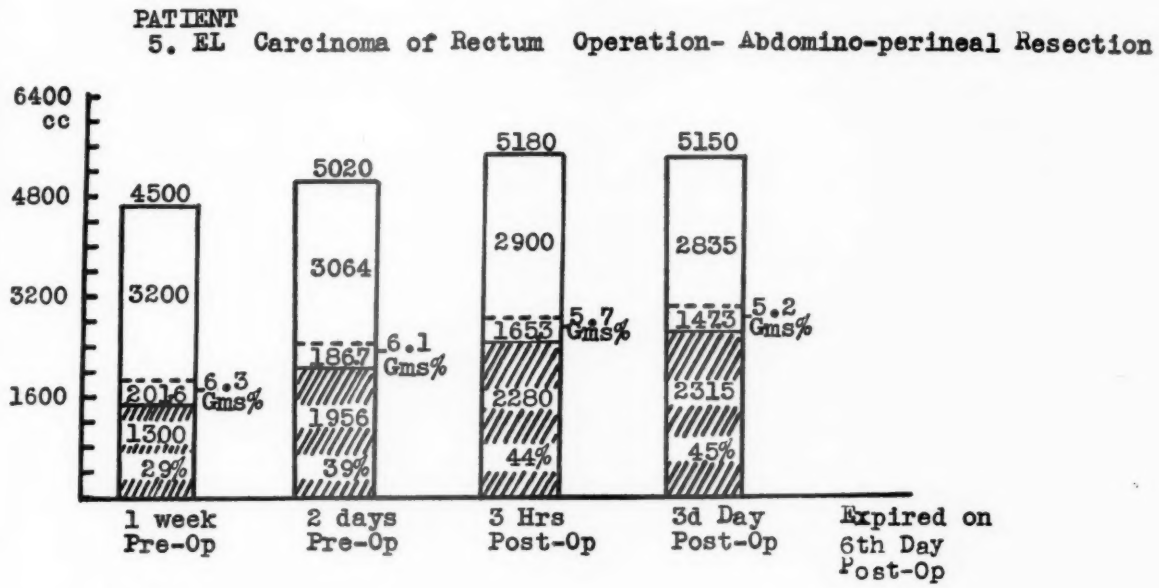


Fig. 4.

ference between success and failure. The narrow margin of compensatory reserve with which these patients are left leaves no room for correcting the error inherent in crude replacement, as, for example, replacement of whole blood when only red cells are required.

Fig. 5.



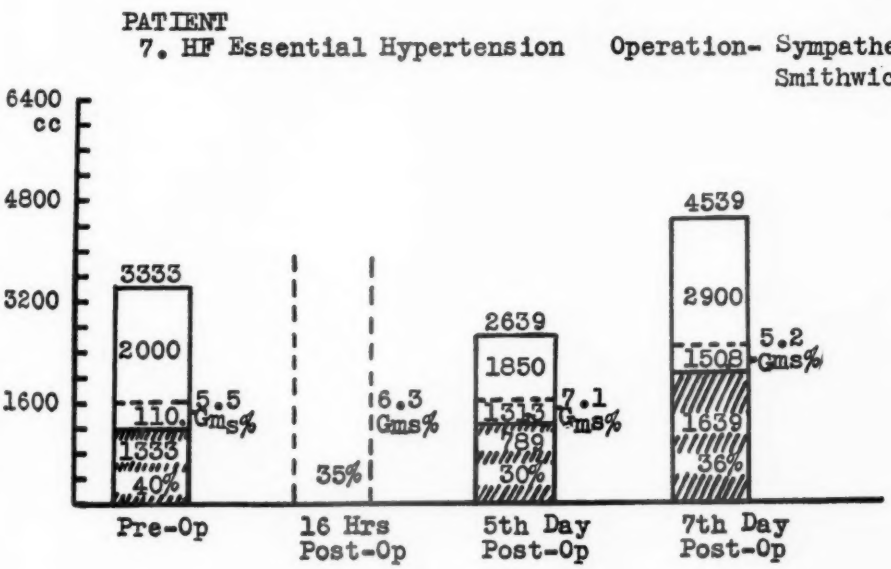


Fig. 6.

Quantitative replacement of the specific fraction in need offers the best hope of success in the very poor-risk group. This applies to both preparation and maintenance. It may mean an infusion of red blood cells or albumin or whole blood as indicated, or electrolytic solutions.

SUMMARY

1. Elderly surgical patients may be protected against cardiopulmonary death and peripheral vascular collapse only by a careful blood volume study. Determination of hematocrit, plasma proteins, and circulating plasma volume is indicated for judicial parenteral therapy.

2. The circulatory system should be stabilized throughout the surgical course and the optimum blood level should be maintained by specific replacement of the blood fraction required.

3. The normal compensatory reserve of vital organs cannot be relied upon to correct the errors of crude replacement therapy.

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FIBROSARCOMA

A Clinical and Pathological Study of Sixty Cases

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IN THIS paper are summarized the clinical and pathological features of 60 cases of fibrosarcoma occurring over a 17 year period at the Presbyterian Hospital, Woman's Hospital, and Elizabeth Steel Magee Hospital. All cases, regardless of anatomic site of origin, were included.

From 1930 to 1947, the diagnosis of fibrosarcoma was made 75 times. The diagnosis was confirmed by re-examination of tissue sections in 60 cases, which form the basis of this report. Of the remaining 15 cases, sections were not available in 10, 2 were reclassified as malignant melanoma, 1 as bronchiogenic carcinoma, 1 as Ewing's sarcoma, and 1 as rhabdomyosarcoma.

GENERAL FEATURES

Of the 60 patients, 23 were males and 37 were females. This is at variance with the reported incidence of a 2 to 1,[1] 1.5 to 1,[2] and 1.6 to 1[3] preponderance of males over females. Only 4 patients were colored, the remaining 56 being white. The age incidence is recorded in Fig. 1.*

ANATOMIC SITE OF ORIGIN

In Table I, these tumors are classified according to their anatomic site of origin. While fibrosarcomas have been reported as arising from almost every tissue of the body, their predominating origin from deep fascial planes and from muscle and nerve sheaths of the trunk and extremities is exemplified by this group of cases. Of particular interest in the group of visceral tumors are 3 unusual cases. We have been able to find but 3 reported cases of fibrosarcoma of the epididymis[4] to which we add one further case. The occurrence of a fibrosarcoma primary in the lung is rare. One such case, in which autopsy was performed, is here included. In one case, the tumor arose from a benign meningioma.

ETIOLOGY AND ASSOCIATED LESIONS

As with tumors in general, the cause of fibrosarcomas is unknown. The relationship of trauma has been a point of controversy; the theoretical conception of traumatic origin bears considerably more validity in this than in most other malignant tumors in view of the predominant role of the fibroblastic cell in posttraumatic repair activity. Ewing[5] described 6 postulates, the fulfillment of which is necessary before trauma can be ascribed as etiologically related. These postulates are (1) authentic trauma, (2) trauma of sufficient severity, (3) previous integrity of the part, (4) the area of injury must correspond with the site of the tumor growth, (5) the date of appearance of the

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*These figures do not reflect the general incidence of the lesion inasmuch as cases from the Children's Hospital are not included in this series.

tumor must be consistent with the date of the injury, and (6) a definite diagnosis of malignancy must be established. While trauma was a definite part of the history in 6 cases in this series, in only one were Ewing's postulates met. In this case, a sledge-hammer blow to the right thigh was followed in 4 months by the appearance of a fibrosarcoma established by biopsy examination.

Two cases in this series originated in patients with multiple neurofibromatosis. In each case, the primary disease was known to have been present for at least 10 years. One case appeared in the base of a varicose ulcer of the leg, and

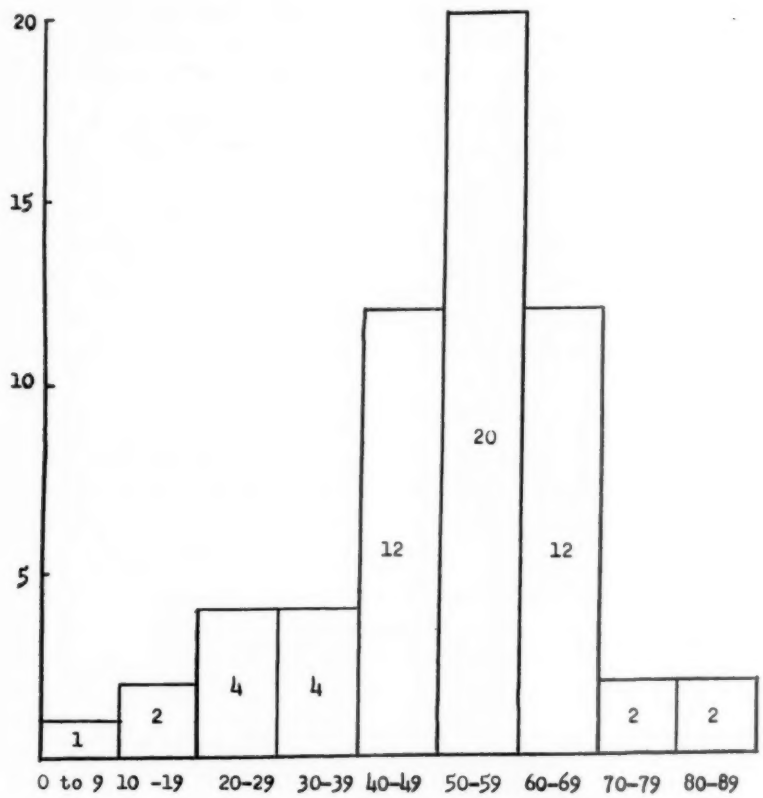

Fig. 1.—Age incidence in 59 cases of fibrosarcoma.

in this instance the ulcer was known to have been present for 15 years. In 3 cases, the sudden rapid enlargement of a pre-existing small tumor mass of 32, 20, and 6 years' duration was noted. These are considered to be examples of sarcomas developing from originally benign fibromas. One case was associated with bilateral mammary carcinoma, the fibrosarcoma being discovered in a left mastectomy scar at the time the patient was prepared for a right radical mastectomy.

Of unusual occurrence is a case of fibrosarcoma appearing in one of the bone lesions of a patient with osteitis fibrosa cystica secondary to a parathyroid adenoma.

Thus, in 9 of the 60 cases, factors bearing potential etiological relationship to the occurrence of the sarcoma were recognized.

TABLE I. ANATOMIC SITE OF ORIGIN OF 60 CASES OF FIBROSARCOMA

Extremities		15
Upper	1	
Lower	14	
Head and Neck		10
Head	4	
Neck	6	
Trunk		11
Abdominal wall	2	
Otherwise	9	
Retroperitoneal		8
Visceral		14
Ovary	6	
Breast	2	
Ascending colon	1	
Epididymis	1	
Bladder	1	
Meninges	1	
Lung	1	
Undetermined	1	
Undetermined		2
Total		60

THE CLINICAL COURSE

The clinical course of these tumors is unpredictable and one of great variability, dependent, in addition to the growth peculiarities of the tumor itself, on its anatomic site. The chief complaint was usually that of a palpable tumor mass. For the most part, the primary tumors were superficially located (39 of 60 tumors); an average time interval of 11 months transpired between the appearance of the mass and the diagnosis. In 18 patients pain was a prominent symptom. Pain was the presenting symptom in many of the retroperitoneal and visceral tumors. The duration of symptoms varied considerably from several weeks to 32 years. The course of untreated patients was uniformly fatal, death resulting from widespread metastases, malnutrition, intercurrent infection, or massive hemorrhage. The average time interval from diagnosis to death was 17½ months, with variations up to 11 years. The average duration of the untreated patient from the onset of the first symptom to death averaged 31½ months with variations from 6 months to 23½ years. The patients with a prolonged course were those whose malignant tumor arose from a pre-existing benign lesion of several years' duration.

While biopsy is an accepted procedure in establishing a diagnosis, this procedure is not without hazard. Complications of biopsy included uncontrollable arterial hemorrhage from the biopsy site accounting for the death of 1 patient 15 days postoperatively, and growth of the tumor into, and separation of, the surgical incision with ulceration and fungation.

PATHOLOGIC FEATURES

Grossly the tumors in this series presented the usual well-known features of fibrosarcoma with variations from the firm fibrous character of the well-

differentiated tumors to the soft fleshy hemorrhagic tissue of the more anaplastic types. In many there was an apparent sharp demarcation from normal structures suggestive of encapsulation. In other cases, invasion of surrounding structures was a prominent feature. The largest of the tumors weighed 4,560 Gm. and measured 27 by 20 by 15 cm.

Histologically, these tumors varied in cellularity, amount of stroma, vascularity, pleomorphism, cell maturity, and frequency and character of mitoses. A histologic grading based on these features was made. All cases were placed in one of four categories, and varied from the acellular tumor, with few mitoses, no giant cells, and uniform tumor cells, classified as Grade I, to the cellular, pleomorphic, anaplastic tumor with many atypical mitoses and giant cells, classified as Grade IV. Variations between these were classified as II and III.

Sections from various parts of the same tumors varied considerably because of edema, degeneration, and necrosis. Discounting such factors pertaining to circulation and viability, any area is generally representative of the entire tumor and the most cellular of such areas was used for grading.

As shown in Fig. 2, there were 6 classified Grade I; 31 Grade II; 20 Grade III; and 3 Grade IV.

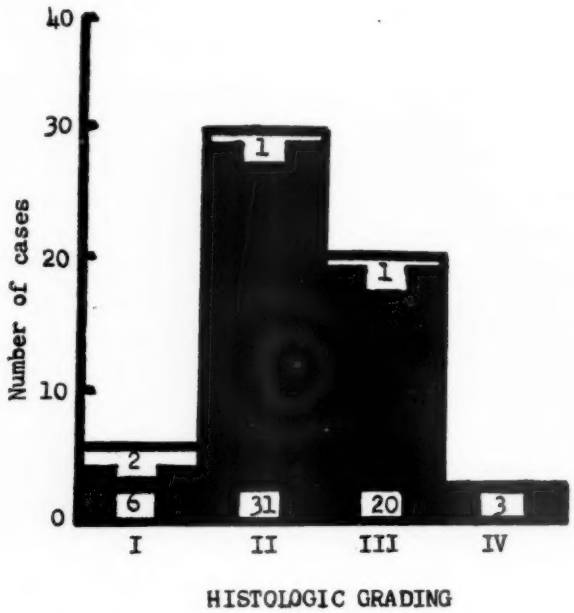

Fig. 2.—Correlation of histologic grading with 3 year survival. (The unshaded column represents 3 year survivals. There are 8 patients living under the 3 year period.)

RECURRENCES

Of 21 patients subjected to surgical excision, 11 are known to have developed recurrences. All recurrences occurred within 1 year of excision of the primary growth. Of these, 8 are known to be dead. Of the remaining 3, a second radical resection was done recently in 2, and in 1, no follow-up information is available. Characteristic of these tumors is their recurrence follow-

ing repeated resection, and their ultimate fatal outcome due to distant metastases. This is well exemplified by a tumor of the foot, resected locally 5 times, and eventually causing the patient's death by abdominal metastases 11 years after primary resection.

While the vast majority of recurrences occur within 1 year following primary resection, a case recurring as late as 15 years following primary resection has been reported.[3] In a large series of cases reported by Warren and Sommer,[6] the longest interval between primary excision and recurrence was 3 years.

While, in general, recurrent tumors are of the same grade as the primary tumor, in 3 cases a progressive increase in degree of malignancy was demonstrated with each successive recurrence.

METASTASES

Death is usually due to distant metastases. While blood-borne metastases are the rule, involvement of regional lymph nodes as seen clinically occurs in approximately 5 per cent[6] of reported cases. In this series of 15 tumors of the extremities, regional lymph node metastasis was found in 1 case. The autopsy findings in 7 cases of fibrosarcoma in this series revealed metastatic lesions of the lungs in 4 and involvement of regional lymph nodes in 3 cases, of which 2 were associated with a general sarcomatosis. In 1 autopsied case, only direct extension to the thyroid gland and adjacent areas was present, with no distant metastasis. This patient died of pneumonia.

COURSE AND RESULTS OF THERAPY

Of the 60 patients here reported, 37 were followed to death, 12 are living, and follow-up data were not available in 11 cases. Of the 37 patients followed to death, 7 died in the immediate postoperative period; in 1 case in which autopsy was not done, the significance of the sarcoma could not be fairly evaluated due to an associated advanced carcinoma of the breast.

Treatment consisted of radical surgery, including wide local excision or amputation in 21 patients, local excision and x-ray therapy in 8 patients, and x-ray therapy alone in 12 cases. In 16 patients, biopsy was performed, but no therapy instituted. Of 21 patients treated by radical surgery, 10 are living, 3 being 3 year survivals and 1 a 5 year survival. The remaining cases are too recent to evaluate, including 2 which represent radical excisions of recurrent tumors. Local excision combined with x-ray treatment resulted in 1 long-term survival. This patient is alive with no recurrences 5 years and 11 months following therapy. X-ray therapy alone has resulted in no cures. One patient treated by irradiation alone survived 6 years and 1 month before death from pulmonary metastases.

PROGNOSIS

All data were evaluated in an attempt to secure findings of prognostic significance. According to Broders and associates,[1] the type of tumor, the graded degree of malignancy, the location of the primary tumor, natural resistance and age of the patient, and the diligence with which treatment is in-

stituted are all of prognostic significance. Recurrence is of grave significance. The known duration of the tumor before diagnosis is of an uncertain significance in evaluating prognosis. According to Carroll and Martin,[7] those patients with a history of a tumor of long duration seem to have a better chance of survival than those of short duration. This is refuted by Bick,[8] whose experience was more favorable with tumors of relatively recent occurrence. In this series, duration of the tumor prior to the onset of therapy revealed no correlation with clinical course and offered no aid in prognosis.

Prognosis based upon histologic grading is commonly attempted. Opinion of its reliability varies considerably. Bick[8] was unable to establish correlation between histologic structure of a fibroblastic tumor and its relative malignancy, whereas Broders and co-workers,[1] and Wilson[3] found a close parallel between the prognosis and the histologic character of the sarcoma. It is common experience that the number of mitoses alone is an unreliable index of the degree of malignancy, and that the degree of cellularity and anaplasia, the presence or absence particularly of multinucleated tumor giant cells, are of equal or greater importance.

The period of survival of untreated patients was not influenced by the anatomic site of origin. The average duration of life from the onset to death in all patients was 31½ months.

Using the system of grading previously referred to, a correlation with clinical course was attempted. Fig. 2 shows the results of such a study. In greater detail, of 6 patients with Grade I tumors, 4 are living, 2 surviving beyond 3 years.

Of 31 patients with Grade II tumors, 4 are living, 19 are known to be dead, and in 8 no follow-up information is available. Of the 4 living, only 1 has survived beyond 3 years. The average survival time from onset to death was 34.5 months.

Of 20 patients with Grade III tumors, 3 are living (5 years, 2 years 4 months, and 22 months) following resections. Of the remaining, 12 are known to be dead, and in 4 no follow-up information is available. The average survival time was 16.0 months.

Of those having Grade IV tumors, 1 is known to be dead, 1 has been living for 2 years with recurrence, and in 1 no follow-up data are available.

In general, one might say that the correlation between the histologic grading of the tumor and the clinical course was, at best, only generally helpful, and no close parallel could be detected.

In our experience, the histologic grading reflects the rate of tumor growth but it cannot be applied in the individual case as an accurate prognostic index.

SUMMARY AND CONCLUSIONS

1. The clinical and pathological features of 60 cases of fibrosarcoma are presented. Single cases of fibrosarcoma primary in the epididymis and lung are represented in this series.

2. In 9 cases associated factors of possible etiological significance were uncovered. These include trauma, chronic irritation, and pre-existing benign lesions. The development of malignancy in a pre-existing benign tumor was the most significant etiological factor in this group.

3. Of 60 patients, 37 were followed to death, 12 are living, and no follow-up information was available in 11. The average length of survival after the appearance of symptoms was 31½ months, and the average time interval from the appearance of symptoms to diagnosis was 11 months.

4. Of the 12 living patients, 4 survived for more than 3 years. Of these, 3 were treated by radical excision and 1 by local excision and x-ray. X-ray alone has resulted in no cures.

5. In our experience, the histologic grading of these tumors reflects the rate of tumor growth but it cannot be applied to the individual patient as an accurate prognostic index.

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SIMPLE EXCISION OF LUNG ABSCESS

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IN SPITE of the paucity of the material, it was thought that a summary of three patients, in each of whom a lung abscess was excised, might be of interest since it represents both a departure from and a refinement of the more recently advocated methods of pulmonary resection in the treatment of lung abscess. The ease of excision, together with the lack of postoperative disability or complications, was pleasantly surprising, and I might say, this reaction was shared by others who observed these patients. The object of this report is to outline our present method of treating the single lung abscess, emphasizing, in particular, the feasibility of their excision under certain conditions. This method is a further application of the principle emphasized by Churchill and Belsey[1] that surgical treatment of suppurative disease should conserve the maximum amount of normal lung tissue so as to insure the greatest ventilatory efficiency.

The gravity of lung abscess in the past is best reflected by its mortality of 35 per cent, reported by Graham, Singer, and Ballon[2] for a collected series of cases. Because of this high mortality, Heuer[3] as early as 1920 performed early drainage in a small group of cases with surprising success. Neuhof and Touroff[4] firmly established this method as by far the best therapy for the acute putrid abscess, by achieving a reduction in mortality to 5 per cent.

Although this treatment proved remarkably successful in saving life, the complications of persistent bronchocutaneous fistula or bronchiectasis at the site of the previous abscess have long been recognized as serious objections to simple drainage. Furthermore, the lung involved by an abscess is rarely restored to normal but harbors either an area of fibrosis, more vulnerable to future infection, or a localized bronchiectasis, always potentially dangerous.

In the past few years the antibiotics have greatly influenced the incidence, the course, and the therapy of the single lung abscess so that now not only do we see fewer, but also they are far less dangerous. Today, the initial sepsis and toxicity, which in the past so frequently led to death, are as a rule readily controlled by antibiotics in conjunction with other conservative measures. This treatment has proved so successful that early surgical drainage is rarely necessary, and, instead, conservative measures may be used with expectation of an initial satisfactory response. Some of these patients progress to complete recovery; others are left with a residual chronic abscess that may cause few constitutional symptoms but that prevents resumption of normal activities.

For this latter group, surgical removal of the portion of the lung containing the abscess, either in the form of a lobectomy or a segmental resection, has been advocated by some. We have now in three instances dissected the abscess out of the normal lung tissue, thus preserving the maximum amount of the normal lung. It so happens that in each of these patients the abscess represented a different stage in the life history of the disease, so that a wide range of

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therapeutic indications were covered. Although no acute lung abscess in its early phase has been treated by excision (and at present it is not felt that such an abscess should be so treated), experiments are now being done in animals to determine if it is feasible. Brief summaries of the cases follow.

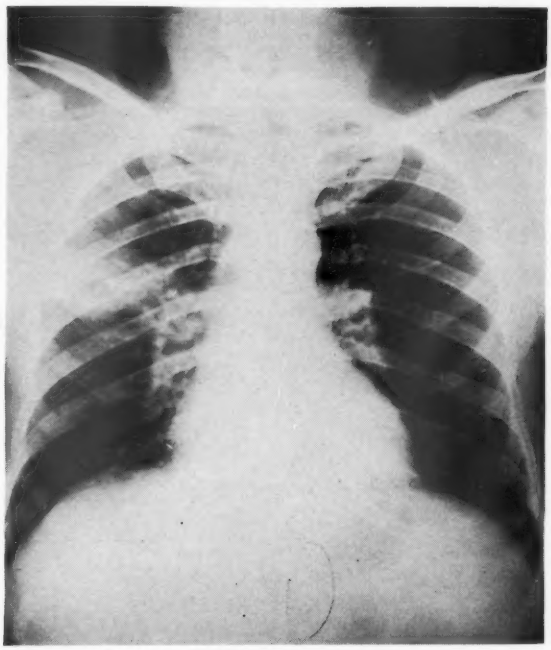


Fig. 1.—Case 1.

The first patient, N. F., a 41-year-old white man, was admitted with typical symptoms, signs, and x-ray findings (Fig. 1) of a lung abscess of three weeks' duration that followed a small abscess in the neck. Sepsis and toxicity were effectively controlled by conservative measures and antibiotics, but with each attempt to increase his activities, symptoms recurred, so that after a twelve-week period an abscess still remained. With the purpose of performing either a segmental resection or a lobectomy, the chest was opened through a posterior lateral incision. It was found that an abscess, apparently arising in the inferior segment of the upper lobe, had broken into the interlobar septum between the upper and middle lobes and had caused a small secondary abscess of the middle lobe. It was thought that lobectomy or even segmental resection would sacrifice too much normal lung tissue, so it was decided to attempt an excision of the abscess. Surprisingly, a plane was easily established between normal lung and the wall of the abscess. There was little bleeding from the surface of the lung, and only a small bronchus and accompanying vessel at the apex of the abscess required ligation. A free pleural graft was placed over the divided bronchus and a catheter inserted for drainage. The postoperative course was without complication, and the patient has remained well during the past eighteen months.

Several points illustrated by the course and findings in this patient merit special comment. First, the initial prompt and satisfactory response to treatment demonstrated that the bacterial flora of the abscess were reasonably sensitive to the antibiotics, a matter of great importance since it provided adequate assurance that the serious postoperative complications, such as a rapidly progressive pneumonia or fulminating empyema, would be avoided. The abscess was opened, its contents aspirated, and, then its wall dissected from the con-

tiguous lung, in much the same fashion as in the dissection of a hernial sac. In spite of gross contamination of the pleura and the trauma to the normal lung adjacent to the abscess wall, the postoperative course was smooth and without complications.

Second, the anatomic segment of lung involved provided both the clue as to how the abscess developed and explained the ease of excision. The events that led to the formation of the abscess may be postulated somewhat as follows:

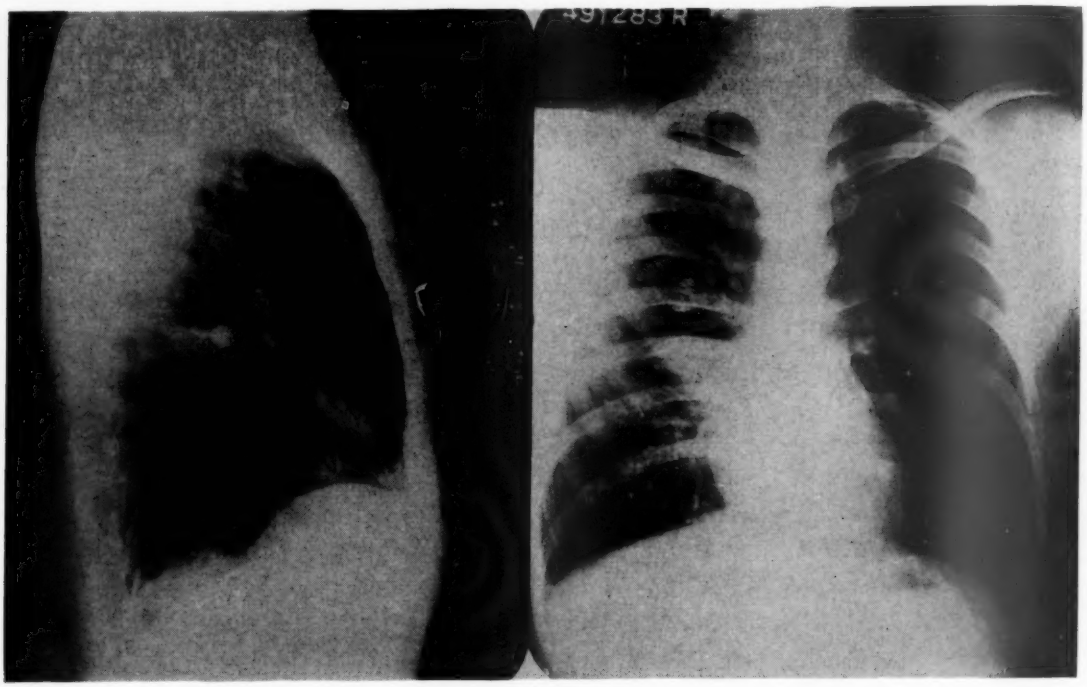


Fig. 2.—Case 2.

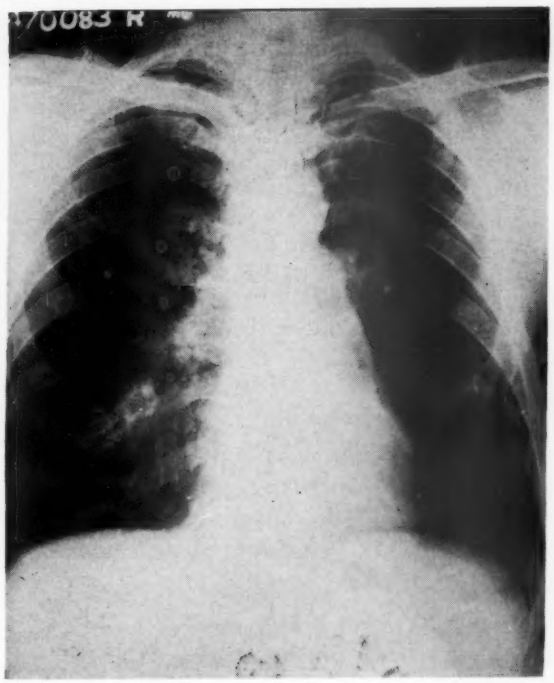
an infected embolus, originating from the cervical abscess, lodged in the branch of the pulmonary artery supplying a segment of lung, which led to an infected infarct that progressed to putrefaction and excavation. This evolution follows the notion of Holman[5] and Cutler and Schlueter[6] regarding the etiology of lung abscess and is mentioned particularly because, in contrast to the second case, the abscess followed an atypical pneumonia and yet, as will be pointed out, a similar anatomic bronchovascular segment was involved.

As was mentioned, the abscess wall was dissected free of the normal lung with ease, and only at the apex, or hilar aspect of the abscess, were bronchi or vessels of any note transected—additional evidence that the original anatomic site of the abscess was a true bronchovascular segment.

Third, although the abscess was entered and the pleural cavity grossly contaminated, no empyema resulted, further evidence of the remarkable protection against infection offered the pleura by the antibiotics.

The second patient, P. P., a 24-year-old white man, entered the hospital because of symptoms and x-ray findings (Fig. 2) of a chronic lung abscess of one month's duration. Although the illness originated with general malaise, fever, and a productive cough, he never

was critically ill. The sputum, always purulent, averaged 20 to 30 c.c. daily at the onset but rapidly decreased to 8 to 15 c.c. daily. On admission, the patient was well nourished and not ill appearing, and examination was negative except for the chest roentgenograms. At operation, an abscess in the dorsal apical segment of the lung was found in addition to an interlobar empyema, the latter containing approximately 20 c.c. of thick yellow pus. The thickened pleura lining the empyema cavity was dissected from the lung as in a decortication, and the abscess was literally shelled out of the lung. Again, a single bronchus and a sizable blood vessel at the apex of the abscess near the hilum were the only major structures that required ligation, closure, and fixation. These were covered with a free pleural graft. Again, the postoperative course was uneventful and without complication despite obvious contamination of the pleural cavity.



Figs. 3 and 4.—Case 3.

The abscess in this second patient, on contrast to the first, followed a pneumonia rather than an infected infarct, and yet the pathology found in each case was much the same. It would seem that whatever the original insult, whether pneumonia or infected infarct, thrombosis of the pulmonary vessel supplying a pulmonary segment precedes and leads to the formation of the abscess which is confined to a true bronchovascular division of the lung.

The third patient, J. B., a man of 47 years, was admitted because of weakness, a mild, nonproductive cough, and x-ray findings (Figs. 3 and 4) of a small density in the right lower lung field. The time or origin of the abscess was difficult to fix. The patient had always been well except that one year previously he had had fever and night sweats for approximately three weeks, from which he gradually recovered. Exploration was done because of an undiagnosed pulmonary lesion, which was considered a possible primary carcinoma. At operation a globular mass on the superior surface of the lower lobe was found. It was shelled out of the normal lung tissue with ease and with practically no bleeding except from the satellite vessel, accompanying the small occluded bronchus leading to the abscess. The abscess, obviously of long standing, contained caseous inspissated pus, and the adjacent lung appeared quite normal.

Although the etiology of the abscess in this patient is uncertain, again the anatomic part of the lung involved was a true bronchovascular segment.

The experience gained from these three patients demonstrates the value of excision of a lung abscess under certain circumstances, and leads one to several conclusions.

First, in the past, all our efforts in treatment were directed toward preventing the formation of a rigid fibrotic abscess wall, or, if one had already been formed, it was carefully avoided and given a wide margin at operation. Now, this capsular wall serves the useful purpose of marking the boundary for excision.

Second, in each of these cases the abscess had as its anatomic origin a bronchovascular segment of lung, characterized by a single demonstrable bronchus with its satellite vessels leading into the apex of the abscess.

Third, apparently the etiology of an abscess may be either embolic or postpeumonic in origin. In either case, the pulmonary artery supplying a bronchovascular segment is occluded by an embolus or thrombosis that precedes and leads to putrefaction and excavation of that segment of lung.

Finally, as has been repeatedly demonstrated, the antibiotics and chemotherapy afford the pleura, like the peritoneum, an amazing degree of resistance to infection.

SUMMARY

The prerequisites for successful excision may be simply stated as:

1. A single abscess in which lobectomy would sacrifice too much normal lung tissue.

2. The infecting organisms should be reasonably sensitive to antibiotics in order to prevent overwhelming postoperative sepsis and toxicity.

3. A degree of chronicity is desirable to insure both a minimum surrounding pneumonitis and an adequate capsular demarcation of the abscess from the normal lung.

4. The importance of covering the bronchial stump, no matter how small, with either a pleural flap or free pleural graft cannot be overemphasized. This provides for the trapping of blood and plasma about the bronchial stump, which facilitates the normal process of wound healing.

5. The same precautions should be observed as when any type of lung resection is performed; that is, expert anesthesia, careful dissection, adequate blood replacement, and attentive postoperative care with use of antibiotics and chemotherapy.

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PULMONARY LOBECTOMY

An Experience With 110 Consecutive Resections Without Operative Mortality*

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FOREWORD

IT IS a great privilege to have the pleasure of writing an introduction to this article "Pulmonary Lobectomy." With the exception of the first five or six patients who were operated upon by the attending surgeon, the remainder, somewhat over 100 patients, had surgery performed entirely by the residents on the Thoracic Surgery Service of the Bronx Veterans Hospital for the past two and one-half years. Although all of this work was done by the five or six residents on service during this time with the supervision and assistance of the attending surgeons on duty, it was the residents who did the work, prepared the patients for operation, and cared for them afterward. This is an exceedingly good record. The cases were entirely unselected and all of them have had an extremely good follow-up. The figures and the conclusions speak for themselves. This is a fine example of what may be accomplished on a well-controlled teaching service in any hospital. The results noted here can be obtained only by a wholehearted cooperation and friendliness of the entire staff working together and such we have attained in the Veterans Administration Hospital, Bronx, N. Y. The residents for the service are carefully selected and all must have had at least three years of general surgery. They have maturity of judgment and high technical skill. To one who grew up in the "hard way" from the times when lobectomy was associated with horrendous mortality and the dire complications of sepsis and pneumonia, it is indeed gratifying to see this large series carried through with such confidence, care, and low incidence of complications. The work of Meade and Kay at the Kennedy General Hospital during World War II shows what may be expected from a well-run thoracic surgical service. They were fortunate in having the young healthy age group that existed in the Army. In the veterans group, however, there is an infinitely wider spread in age and in severity of disease. But building on all that has gone before and has been made possible by the work of many, our staff has gone steadily ahead. I am happy, therefore, to congratulate all of them upon their very fine work: the residents, the attending surgeons who assisted and instructed them, the anesthesiologists who gave so freely of their advice and time, and the nursing staff.

—*Frank B. Berry,* M.D.

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*Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Pulmonary lobectomy for various morbid conditions of the lung is being performed with ever-increasing frequency, especially since the stimulating reports of both Churchill[1] in this country and Edwards[2] in England. Large series of cases with excellent operative results and low postoperative morbidity and mortality have been reported.[3, 4] This report is conceived with the idea of relating the recent experience of a thoracic surgical service in a large veterans hospital and again emphasizing the relative safety of the procedure.

MATERIAL

This group is comprised of 110 consecutive pulmonary lobectomies for diverse pathology performed on 105 patients in a thirty-two month period from May 1, 1946, to Jan. 1, 1949.* There has been a gradual increase in the operative material during this time. In the first three months but five lobectomies were performed, whereas in the last month, December, 1948, there were seven.

TABLE I. PULMONARY LOBECTOMY, POSTOPERATIVE PATHOLOGIC DIAGNOSIS

Bronchiectasis	64
Chronic lung abscess	20
Tuberculosis	7
Bronchiogenic carcinoma	6
Bronchial adenoma	2
Bullous emphysema	2
Chronic organizing pnuemonia	2
Aspergillosis	1
Boeck's sarcoid	1
Bronchiectasis and tuberculosis	1
Bronchiogenic carcinoma and tuberculosis	1
Bronchiogenic cyst	1
Coccidioidomycosis	1
Granuloma, nonspecific	1
Total	110

Nearly all patients were referred to this hospital from regional offices, other Veterans Administration hospitals, civilian hospitals, or directly from private physicians. They were admitted to the chest medical service in most instances where they were evaluated and any necessary work-up was performed. In many instances they were presented to a combined conference of the medical and surgical consultants and attending surgeons before a final decision as to therapy was reached. The diagnosis was evident preoperatively in the great majority of cases.

Age, Sex, and Race.—There were 104 men patients and 1 woman in the group. Their ages varied from 19 to 63, the average being 35 years. Twenty-four were over 50 and thirty-two were over 40 years of age. Ninety-six were white, seven were Negroes, and two were Chinese.

Follow-up Examination.—Coincident with the reorganization of the hospital under the Dean's Committee, a follow-up clinic was established. From its beginning it has functioned remarkably well. All of the various facilities at the disposal of the Veterans Administration are used so that a patient is seldom lost.

*At the time of submission for publication twenty-four additional lobectomies had been performed without mortality, a total of 134 consecutive cases.

Prior to Dec. 1, 1948, ninety-eight patients were operated upon. Ninety-seven have had follow-up at least once since operation, and many several times. Eighty-seven have been interviewed, examined, and have had chest x-ray pictures at the follow-up clinic since discharge. The data on the remaining ten patients have been obtained by letter. With a follow-up approaching 100 per cent, exceedingly valuable and accurate statistical data should accrue.

PATHOLOGY

Bronchiectasis.—The majority of the operations were for bronchiectasis. All had bronchographic demonstration of the disease preoperatively and decision for therapy was based on persistent symptoms despite active medical therapy. One patient, the only woman in the group, had a calcified lymph node eroding into the left lower lobe bronchus with distal bronchiectasis. This condition was recognized preoperatively by bronchoscopy and a left lower lobe lobectomy performed. A young man had bronchiectasis of the right middle and lower lobe secondary to a foreign body aspirated a few years previously. In a third instance, a case of situs inversus, a left middle and left lower lobe lobectomy was performed for bronchiectasis. Active tuberculosis of the lower lobe was found in addition to the bronchiectasis.

All of the sixty-three patients with bronchiectasis operated upon prior to Dec. 1, 1948, had follow-up at least once since operation. However, it is not within the scope of this paper to report this in detail. Nearly every patient with unilateral disease completely removed at operation has had a good result. Seven patients are rated as poor results. All but one of these has bilateral disease proved by bronchography. Three have been felt to be unsuitable for further surgery either because of age or extent of disease, and the remaining three have been advised to have surgery on the opposite side.

Chronic Lung Abscess.—There were twenty resections of lung for chronic lung abscess. Ten were upper and ten were lower lobe abscesses. Ten were on the right side and ten on the left. All twenty patients left the hospital asymptomatic with the exception of one who subsequently developed pulmonary tuberculosis and is still hospitalized. No evidence of tuberculosis existed in chest roentgenograms or sputum concentrates prior to operation and no tuberculosis was found in the resected lobes in this case. In one patient a large piece of wood was found in the right upper lobe at operation. As a child he had fallen and pierced his neck with a toy wooden spear leaving a small scar. Although this had been noted in the history, a correct preoperative diagnosis was not made and exploration was performed for an unexplained symptomatic upper lobe cavity. The results in this group of patients have been particularly gratifying in view of the usual considerable mortality in this condition.[5] Two cases are too recent for follow-up. One patient has not been located since discharge, one has tuberculosis, and the remaining sixteen are well.

Carcinoma.—Lobectomy for primary carcinoma of the lung rather than pneumonectomy has been performed in a few selected patients. The indications were: (a) localized peripheral tumors without hilar involvement, and (b) little respiratory reserve in poor-risk patients in whom lobectomy was tech-

nically feasible and in whom pneumonectomy would carry an extremely high mortality. There were five cases of peripheral neoplasms. In four of these extensive portions of the chest wall consisting of segments of four or five ribs and intervening structures were removed en bloc with the affected lobe. One patient had a very small peripherally located lesion. Of the five patients with peripheral carcinoma, three are now working full time, one is well but not working, and one has evidence of metastases in both lungs. The remaining two patients were both poor risks with limited pulmonary reserve. Although all visible carcinoma was removed at the time of operation, both died of cancer, one 3½ and the other 4½ months postoperatively. All operations were performed prior to Sept. 15, 1948. In summary, of the seven patients with carcinoma, four are well, with three working, one has metastases, and two are dead.

Tuberculosis.—There were nine instances in which active tuberculosis was found in the resected specimen. In only four of these was the diagnosis made preoperatively and the resection performed as an elective measure for tuberculosis. In two instances the preoperative diagnosis was bronchiogenic carcinoma, and in one chronic lung abscess. In the remaining two cases, active tuberculous lesions of considerable extent were found in addition to carcinoma in one instance and to bronchiectasis in the other. Four of the five patients who had upper lobe resections have had upper thoracoplasty. The five patients who were operated upon prior to January, 1948, have resumed normal activity at home or are working. The other four remain on sanatorium care. There has until this time been no evidence of spread of tuberculosis in any patient. Streptomycin was used prophylactically in all the elective resections. Although a relatively large number of patients with pulmonary tuberculosis are screened and treated at this hospital, the number of resections for tuberculosis has been relatively small.

Miscellaneous Pathology.—The remaining cases are comprised of a variety of conditions. The patient with coccidioidomycosis has been previously reported.[6] A 59-year-old man had a peripheral adenoma removed by left lower lobe lobectomy. Another adenoma which showed invasive characteristics was found to be the cause of a right upper lobe atelectasis of three years' duration. In another instance, an atelectatic right middle lobe was removed and Boeck's sarcoid found to be the basic pathology. Pulmonary aspergillosis verified by culture and tissue section was found in a right upper lobe. Exploration for carcinoma had been done in this patient.

Two patients who had lobectomies for localized bullous emphysema have had subjective relief of dyspnea since operation. In two instances right upper lobe lobectomy done for persistent unexplained atelectasis revealed chronic organizing pneumonia without endobronchial lesion. One of them had marked peribronchial lymphadenopathy which on tissue section showed only chronic lymphadenitis. This patient had been having bouts of chills and fever for three years, together with recurrent and then persistent atelectasis of the right upper lobe.

ANESTHESIA AND BLOOD REPLACEMENT

The importance of maintaining an adequate airway, a dry tracheobronchial tree, and providing sufficient oxygen during and following the operation cannot be overemphasized. All anesthesias were administered by resident doctor anesthesiologists under the supervision of their consultant and attending anesthesiologists. Excellent anesthesia was afforded in nearly all instances. Postoperative bronchoscopy was performed on the operating table in only a few instances, in all of which catheter tracheobronchial suction had failed to clear residual secretions. Care was taken to have the patient adequately anesthetized during bronchoscopy to avoid untoward reflexes.

Blood transfusion was routine in all cases during operation. Properly typed and cross-matched blood was in the operating room at the start of each operation. Blood was begun soon after the incision was made, and by the joint observation and cooperation of the surgeon and anesthetist an effort was made to replace blood loss immediately. The amount usually needed for a lobectomy was 1,500 c.c. The ready availability of large quantities of blood for adequate replacement therapy added much to the safety of the procedure and the speed of convalescence of the patients.

OPERATORS

Nine of the operations were performed by attending surgeons. The remaining 101 were done by the resident surgeon with the assistance of, or under the direct supervision of, the attending surgeons. All operations since January, 1947, were performed by the residents.

TECHNIQUE

In all instances individual dissection and ligation silk technique was used in dealing with the hilar structures. Although a "frozen hilus" was encountered in several cases, no tourniquet lobectomy was performed. By painstaking and sometimes very tedious dissection the hilar structures were individually identified and dealt with in every case. The bronchus was closed in a manner similar to that of Sweet[7] except in some of the earlier cases. A posterolateral approach with resection of a rib was the approach in the lower lobe lobectomies and the majority of upper and middle lobe resections. In seven instances an anterior approach was used through the third interspace with division of adjacent costal cartilages medially and the fourth rib laterally. Twenty-eight patients had upper lobe resections. Fifteen of these had upper thoracoplasty. Intrapleural penicillin and intercostal tube drainage of the pleura were used routinely. In some instances, especially upper lobe and segmental resections, an anterior intercostal catheter was used in addition to the usual posterolateral tube.

Number of Lobes Removed; Bilateral Lobectomy.—Twenty-five patients had more than one lobe removed at one operation and thirteen patients had two entire lobes removed at the same operation. Five patients had staged bilateral lobectomies. All were for bronchiectasis and all were performed at this hospital. At the time of this communication the patients are leading normal lives

without untoward dyspnea. One has 3 to 4 ounces sputum daily, apparently arising from a remaining right lower lobe, the right middle lobe, left lower lobe, and lingula having been removed. This patient was the only one of the five who was not working at the time of the last follow-up. This would indicate that in properly selected individuals bilateral lobectomy is perfectly feasible, does not carry a prohibitive mortality rate, and does not leave the patient a respiratory cripple. All of these charges have been leveled against the procedure and in the minds of many physicians appreciable bilateral bronchiectasis has automatically barred excisional surgery.

Three patients who had had previous lobectomy had further excisional pulmonary surgery on the same side. The first operation had been done at other hospitals in two instances. A 30-year-old man had a right middle lobe lobectomy in the Navy in 1944. Bronchograms at that time had shown bronchiectasis in the right lower lobe as well, but the latter was not thought sufficient to warrant surgery. However, he continued to have 4 to 5 ounces of purulent sputum per day. Following a right lower lobe lobectomy in August, 1948, the sputum disappeared. Saccular bronchiectasis was present in the specimen.

Segmental Resection.—Eleven segmental resections were performed. This includes two cases in which the lingula alone was removed, the left lower lobe having been previously removed. Five of these operations were for bronchiectasis and three were for chronic lung abscess. The result in all cases has been satisfactory. There was one postoperative empyema and no bronchopleural fistula in these eleven cases.

POSTOPERATIVE CARE

The seventy-two hours following operation are crucial. The patient must constantly be protected against anoxia. Prior to operation he is given a lecture on the importance of postoperative coughing and deep breathing. Postoperative tracheal suction after the method of Haight[8] has been practically routine. The number and frequency of aspirations have been individualized to the patient's need, some being better able to rid themselves of accumulating secretions than others. Emergency bronchoscopy in several instances immediately cleared a roentgenologically established atelectasis.

In addition to atelectasis, constant vigilance must be maintained for pneumothorax, bronchopleural fistula, hemothorax, and empyema by frequent physical and x-ray examination. These patients with their nasal oxygen, oxygen tents, underwater drainage, and suction bottles require the best of closely supervised and well-trained nurses accustomed to the postoperative care of major thoracic surgery.

Complications.—Atelectasis, empyema, and bronchopleural fistula have been the most frequent complications. Eighteen patients had postoperative atelectasis. In sixteen there was diagnostic roentgenographic confirmation. In the remaining two, appropriate measures apparently cleared the process before an x-ray picture could be taken. Daily chest roentgenograms were routine for the first three days and were continued as long as the patient's condition warranted it. Atelectasis occurred as late as the twelfth postoperative day, but occurred generally during the first seventy-two hours. Three patients

who had atelectasis subsequently developed empyema. There were twelve instances of bronchopleural fistula. Four of the fistulas were in tuberculosis cases. Nearly all the fistulas were closed early in the postoperative course by open drainage and muscle plasty. In the single case of aspergillosis, a fistula did not become apparent until three months postoperatively. It was easily closed with a muscle flap. In the last twenty operations there were no fistulas and one empyema.

TABLE II. POSTOPERATIVE COMPLICATIONS

COMPLICATIONS	NUMBER	PERCENTAGE
Atelectasis	18	16.4
Bronchopleural fistula	12	10.9
Empyema without fistula	8	7.3
Residual apical pneumothorax	4	3.6
Homologous serum hepatitis	3	2.7
Hemothorax	3	2.7
Brachial plexus palsy (transient)	2	1.8
Parotitis (first postoperative day)	1	0.9
Pulmonary tuberculosis (after resection for lung abscess)	1	0.9
Recurrent laryngeal palsy (unilateral permanent)	1	0.9
Tension pneumothorax	1	0.9
Unexpandable remaining lobes (also included under atelectasis)	1	0.9
Total	55	

There were eight cases of empyema without bronchopleural fistula, all of which were fairly small localized collections responding readily to simple drainage in most instances. One was a localized collection in the tract of the intercostal tube which closed without further surgery.

Four patients have had small apical pneumothoraces which gradually absorbed spontaneously. In two instances emergency thoracotomy was necessary in the early postoperative period because of intrapleural bleeding and clotted hemothorax. Both made otherwise uneventful recoveries. There was a massive collapse of the right upper and middle lobe following a right lower lobe lobectomy with pneumothorax, the latter apparently due to persistent alveolar fistulas. All efforts to re-expand immediately the collapsed lobes were in vain. At operation two weeks later the middle lobe was found twisted inferiorly and posteriorly and lay in the costophrenic sulcus posteromedially near the spine. The upper lobe was adherent to the diaphragm over a large area. Both lobes were decorticated and re-expanded satisfactorily to fill the right hemithorax. Subsequent recovery was uneventful.

Two patients had brachial plexus injury due to pressure or traction on the plexus while in the lateral recumbent position on the operating table. One was a mild limited palsy with complete recovery of function in a few weeks. This man, who had a left lower lobe lobectomy for carcinoma, also developed a left recurrent laryngeal palsy in the early postoperative period for which the explanation was not wholly clear. The second brachial palsy was an upper cord lesion with nearly complete axillary and musculocutaneous involvement. Five months postoperatively he had no objective evidence of nerve damage and was back at school, but had easy fatigue of the arm.

There were three instances of homologous serum hepatitis. Two of these occurred four months postoperatively and the patients were readmitted to the hospital. All recovered.

Sixty-five of the operations were completely without postoperative complication. There were no serious surgical accidents during the operation in any case. Lobectomy was completed in all cases and pneumonectomy was never substituted for lobectomy because of technical error or difficulty.

There were no wound infections in the entire group and no instance of postoperative thrombophlebitis or brain abscess. Anticoagulants were not used and prophylactic femoral vein ligation was not performed.

Operative Mortality.—There were no operative deaths. Two patients died several months postoperatively, both with carcinoma. The remaining 103 are alive. One of these has metastatic carcinoma.

SUMMARY

1. An experience of 110 consecutive pulmonary lobectomies for diverse pathology in 105 patients ranging from 19 to 63 years of age is presented.

2. There was no operative mortality in the series.

3. Adequate follow-up data have been obtained on 99 per cent of the patients whose date of operation warrants follow-up.

CONCLUSIONS

1. In proper hands pulmonary lobectomy constitutes an extremely effective and a relatively benign procedure for the therapy of many common pulmonary conditions.

2. Similarly it is a much safer procedure with regard to morbidity and mortality than is generally realized and as this report would show.

Acknowledgments.—An extremely important role was played by the Department of Anesthesia under Dr. Harold F. Bishop and Dr. Charles L. Burstein, under whose supervision all the anesthesias were administered. We also wish to thank Miss Isabel Guyette, R.N., who together with her excellent staff worked tirelessly and endlessly applying the conscientious and intelligent nursing care necessary to bring all these patients safely through the postoperative period.

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PRIMARY LYMPHOSARCOMA OF THE LUNG

Report of a Case

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LYMPHOSARCOMA as a primary tumor of the lung is rare. The available literature discloses only four previously reported cases. We herewith present a fifth case, primary in the lower lobe of the right lung, without demonstrable metastasis, and treated by right lower lobectomy.

CASE REPORT

A 63-year-old German-born man, a mechanic, entered the University Hospital for the first time April 19, 1949, for investigation and treatment of an abnormal "shadow" found on routine x-ray examination of the chest. He had no systematic complaints whatever, and as far as he was concerned was in vigorous health.

One year previously the "shadow" had been seen on a routine x-ray picture of the chest taken at his place of business. The family physician had advised observation without treatment because of the absence of symptoms. A repeat film five months later (Fig. 1) showed no apparent change in the size, shape, or density of the "shadow" in the right lung field. Although there was no cough, chest pain, weight loss, fever, or malaise the patient was finally prevailed upon to enter the hospital. He performed his regular work up to the time of admission.

The past history was that of sustained good health without significant illnesses or previous hospitalization. There was no known exposure to tuberculosis.

Physical examination at the time of admission disclosed a well-developed and well-nourished white man, appearing his stated age and in apparent good health. The blood pressure was 112/70, temperature 97° F., pulse 80, and respirations 16 per minute. The positive physical findings were restricted to the chest and were minimal in character: slight dullness to percussion of the right chest posteriorly near the base. There was no asymmetry of chest contour or excursion. There was no significant lymphadenopathy in the cervical, axillary, epitrochlear, or inguinal regions. The liver and spleen were not palpable.

Laboratory findings revealed a red blood count of 4.5 million, with a hemoglobin of 13.5 Gm. per 100 c.c. and a white blood count of 10,000 c. mm. The differential count was as follows: neutrophils 70 per cent, lymphocytes 24 per cent, monocytes 4 per cent, and eosinophils 2 per cent. The peripheral blood elements were not abnormal on smear. The urine was negative. Sedimentation rate was slightly elevated: 31 mm. (Westergren) in 1 hour. Total plasma proteins were 7.2 Gm.; albumin 4.3 Gm. per 100 c.c., globulin 2.9 Gm. per 100 c.c.; prothrombin 74 per cent; blood urea nitrogen 14 mg. per cent. Thymol turbidity was normal.

X-ray studies of the chest (Figs. 2 and 3) showed an area of increased density at the base of the right lung posteriorly near the spine. The area of denseness was sharp in outline, homogeneous, and measured 4 by 4 cm. There was no increase of hilar shadows. Comparison with films of nine months and seven months earlier showed no apparent change in the size of the density. Bronchograms revealed partial narrowing of the bronchus supplying the involvel part; however, there was no distal dilatation.

Bronchoscopy showed no significant pathologic changes. Smear of bronchial washings studied showed no malignant cells. Acid-fast smear of bronchial secretion was likewise negative.

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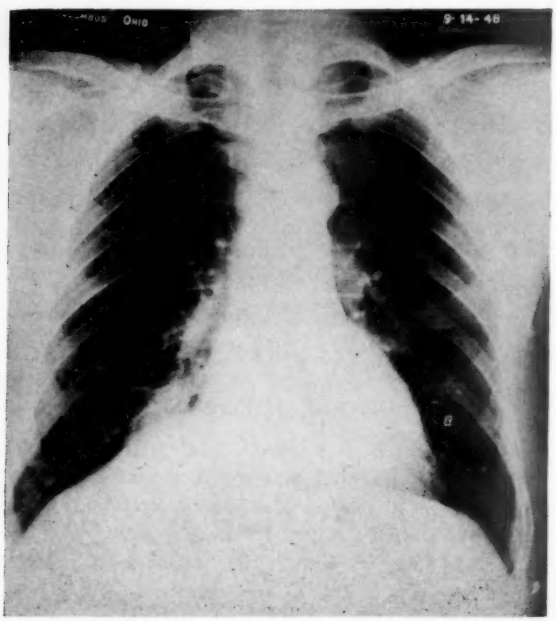

Fig. 1.—Roentgenogram of chest on Sept. 14, 1948, with a shadow in the right lower lobe.

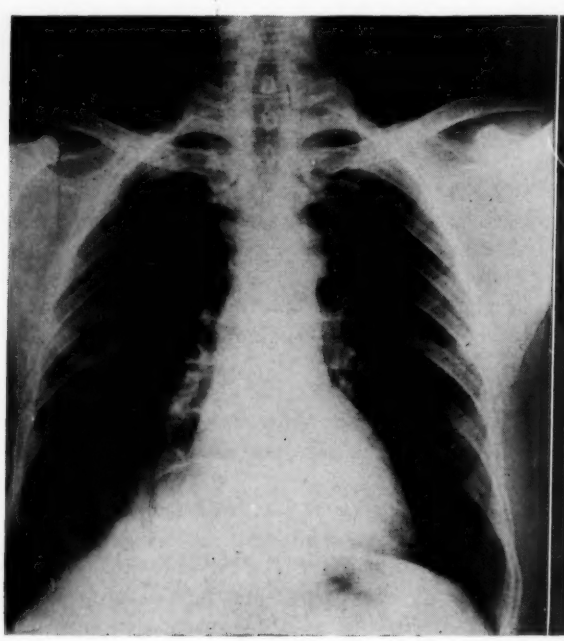

Fig. 2.

Fig. 3.

Fig. 2.—Roentgenogram of chest on April 6, 1949, with the same shadow and no apparent increase in size of lesion.

Fig. 3.—Lateral roentgenogram of chest localizing the lesion in the posterior portion of the right lower lobe.

Sternal marrow studies by the supravital technique did not reveal any evidence suggestive of blood dyscrasia.

An exploratory thoracotomy was advised on the basis that the lesion was probably a neoplasm, although its nature, whether benign or malignant, was uncertain. On April 23, 1949, under sodium pentothal, curare, cyclopropane endotracheal anesthesia, a right thoracotomy through the fifth intercostal space was performed. No pleural adhesions were encountered. In the substance of the posterior segment of the right lower lobe there was an oblong mass which was smooth, firm, and homogeneous. It measured approximately 6 cm. in its greatest diameter. The hilum was free of fixation or lymphadenopathy. A frozen section of the mass was reported as probable lymphosarcoma of the lung. A right lower lobectomy was performed without difficulty by individual ligation technique. A hilar lymph node was removed for study. The postoperative course was uneventful and the patient was discharged on the seventh postoperative day and returned to his occupation three weeks later.

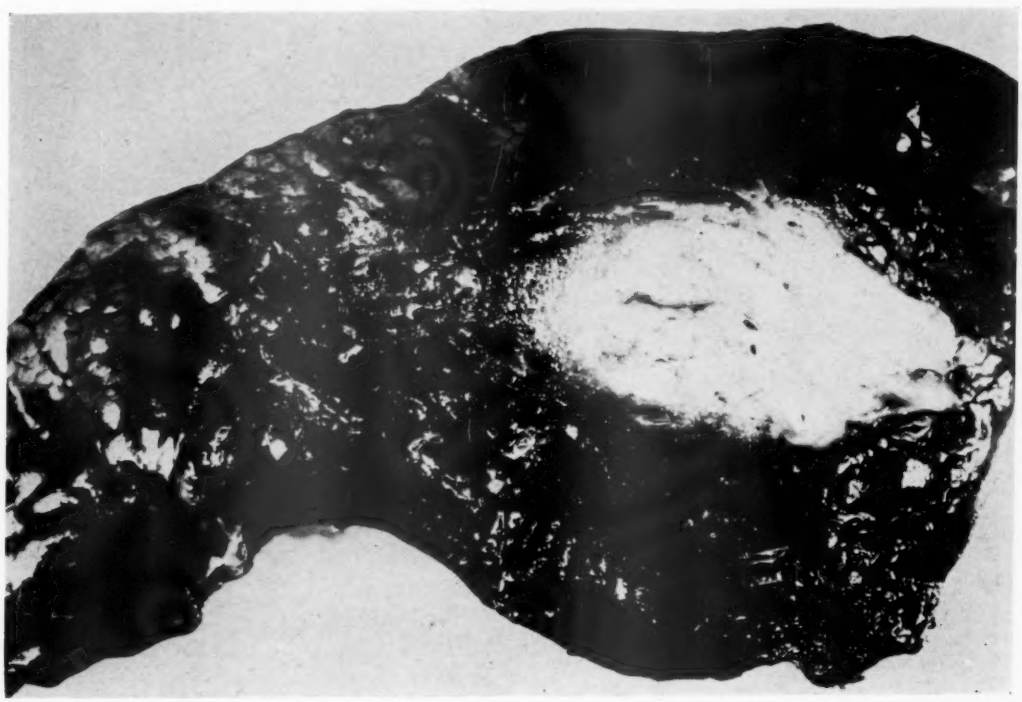

Fig. 4.—Photograph of gross specimen.

Pathology Report.—

The specimen (Fig. 4) consisted of the lower lobe of the right lung which weighed 245 Gm. The pleural surface was smooth. One of the secondary bronchi opened into an ovoid tumor mass 8 by 4 by 4 cm. which was pale gray, homogeneous, and unencapsulated. The lining of the bronchus was smooth but irregularly elevated, and this bronchus traversed the entire tumor. The edges of the tumor extended into the surrounding parenchyma for a depth of 8 mm. Microscopic sections (Figs. 5 and 6) of the tumor showed sheets of small round cells having the appearance of lymphocytes. These cells extended through the bronchial wall, under the lining epithelium of the bronchus. Mitoses were present on an average of one in every eight or ten high-power fields. The tumor cells were separated by a small amount of reticular stroma. Small capillaries were noted throughout the tumor. Microscopic sections of the hilar lymph node showed only reticulum-cell hyperplasia.

Fig. 5.

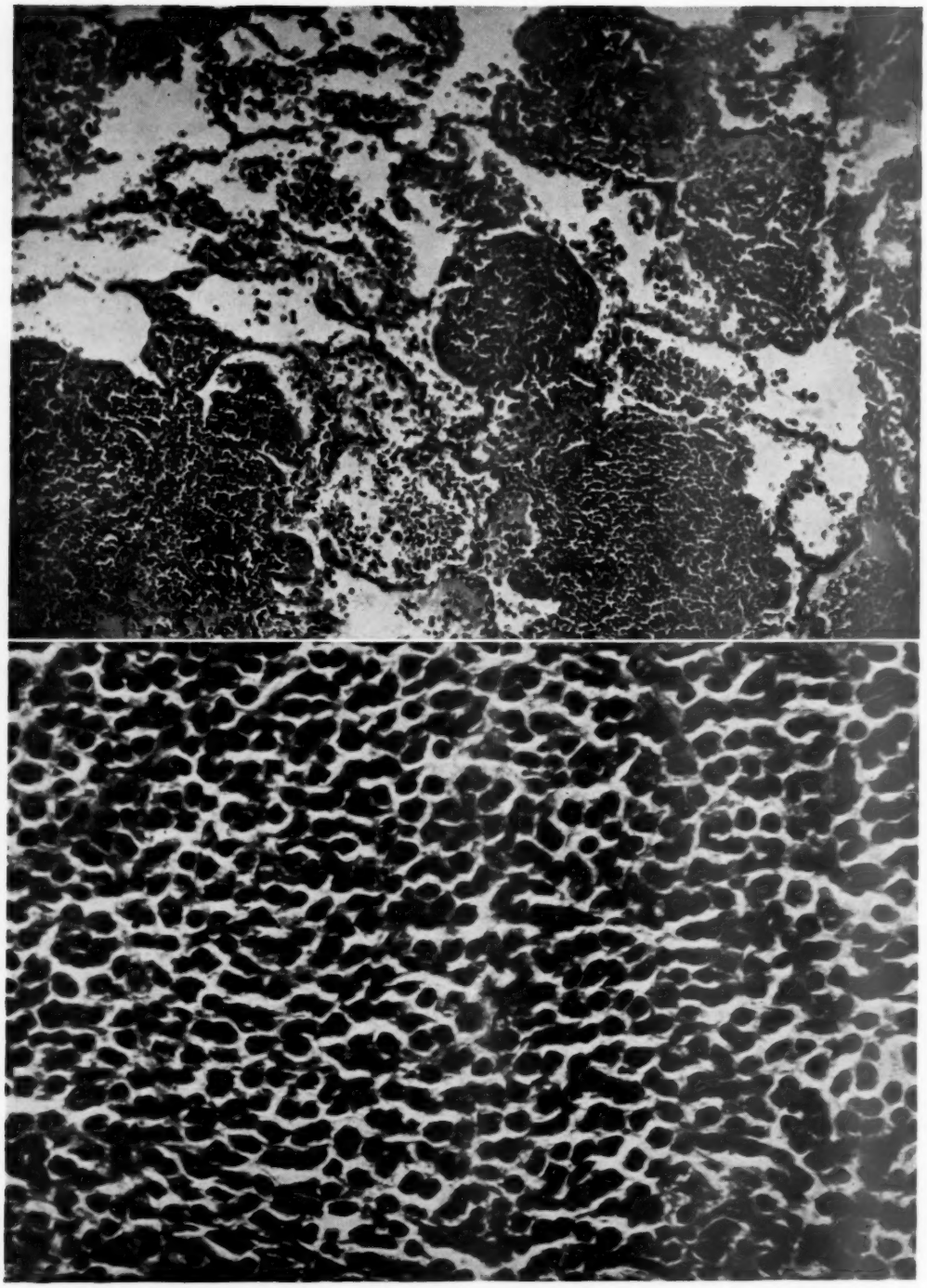

Fig. 6.

Fig. 5.—Photomicrograph (×50) of lesion showing invasion of lung parenchyma by cellular tumor.

Fig. 6.—Photomicrograph (×700) of same lesion demonstrating the lymphocytic type of lymphosarcoma.

DISCUSSION

Of the four cases previously described, in two the lymphosarcoma was apparently limited to the lung,[1, 2] in one it had involved the opposite lung,[3] and in one it had metastasized to sternum, ribs, and liver.[4]

In this case there was no evidence of metastasis, including hilar lymph nodes, bone marrow, and peripheral blood. It is noteworthy that the lesion was slowly growing, as shown by serial x-ray pictures, and that metastasis had not occurred despite the existence of the tumor for at least nine months. This case, like those reported previously, was of the lymphocytic type. It would seem that primary lymphosarcoma of the lung is a definite entity which is relatively slow growing and which is usually diagnosed at exploratory thoracotomy performed for a suspected carcinoma.

SUMMARY

A case of a small, primary lymphosarcoma of the lower lobe of the right lung is presented, which has been treated by right lower lobectomy. This lesion had not increased in size in one year as proved by serial x-ray pictures of the chest. There was no evidence of extension of the malignant process to any other part of the body, including the bone marrow, mediastinal lymph nodes, and peripheral blood.

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THROMBOEMBOLIC COMPLICATIONS IN SURGICAL PATIENTS

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AN ANALYSIS was made in 1946 of the thromboembolic complications on the surgical services of the Hospital of the University of Pennsylvania during the period from 1925 to 1945.[1] The incidence of fatal pulmonary embolism in 67,402 operations was 0.08 per cent (about 1 in 1,200 operations). Ninety-two per cent of the patients who died as the result of pulmonary embolism were over 40 years of age. Although in 1946 there were strong proponents of each of three methods for reducing thromboembolic complications (early ambulation, proximal vein ligation, and anticoagulants), the statistical evidence which had accumulated did not establish the superiority of any one of these methods. In addition, certain limitations of each method had become apparent. It was decided, therefore, to utilize all three methods at the Hospital of the University of Pennsylvania in addition to general prophylactic measures, in an attempt to reduce the incidence of thromboembolic disease. The program adopted is shown in Chart 1. The measures outlined have been carried out during the past three years, in so far as possible, on the general surgical, urologic, and neurosurgical services. The thromboembolic complications occurring during this period have been analyzed and the results are herein reported.

INCIDENCE OF THROMBOEMBOLIC COMPLICATIONS

From July 1, 1946, to July 1, 1949, there were 17,114 general surgical, urologic, and neurosurgical procedures performed in the operating rooms at the Hospital of the University of Pennsylvania. During this period fatal pulmonary embolism occurred in 22 patients, an incidence of 0.128 per cent (1 in 778 operations). Only fatal embolisms confirmed at post-mortem examination were included. Five other patients died following the occurrence of symptoms and signs suggestive of embolism but, since post-mortem examination was not performed, they were not included in this analysis. Twenty-four patients had symptoms and signs which warranted a diagnosis of nonfatal pulmonary infarct, an incidence of 0.14 per cent (1 in 713 operations). In addition, 76 patients had clinical signs of phlebothrombosis or thrombophlebitis. The incidence of all forms of thromboembolic disease during the three-year period was 0.71 per cent (1 in 140 operations). Fatal embolism accounted for 7.5 per cent of all surgical deaths.

FATAL PULMONARY EMBOLISM

Since fatal embolism caused 7.5 per cent of all deaths there was interest in learning why the measures employed did not prevent these deaths. Clinical data thought to be pertinent to the thromboembolism problem were

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CHART 1. MANAGEMENT OF THROMBOEMBOLIC DISEASE; MEASURES USED AGAINST THROMBOEMBOLIC DISEASE FROM 1946 TO 1949

A. Prophylaxis
  (1) Routine measures: early ambulation, compression bandages, deep breathing and leg exercises, prompt replacement of blood loss, avoidance of abdominal distention and of heavy sedation, prevention of dehydration, electrolyte imbalance and hypotension
  (2) In patients in whom there is an unusual risk of a thromboembolic complication: prophylactic use of anticoagulants and prophylactic superficial femoral vein ligation; patients to be selected by the chief of service

B. Treatment
  (1) Phlebothrombosis: bilateral superficial femoral vein ligation or anticoagulants, at the discretion of the chief of service
  (2) Acute thrombophlebitis: lumbar sympathetic block or anticoagulants
  (3) Extension of thrombus proximal to femoral vein: anticoagulants
  (4) Suppurative iliofemoral or pelvic thrombophlebitis: ligation of the iliac veins or vena cava
  (5) Pulmonary infarction without dyspnea: bilateral superficial femoral vein ligation or anticoagulants at the discretion of the chief of service
  (6) Massive pulmonary embolism: heparin 50 mg. intravenously at once; in addition, atropine, papaverine, oxygen, and morphine

recorded with unusual care during the three-year period and were therefore suitable for an accurate analysis of several contributory factors.

Age and Sex.—Only 3 of the 22 fatal embolisms occurred in patients under 40 years of age (13.6 per cent). One followed a craniotomy for recurrent meningioma in a 35-year-old man, one a ventriculogram in a 23-year-old man with tuberculous meningitis, and one a Blalock operation for the tetralogy of Fallot in a 14-year-old boy with a preoperative hemoglobin level of 150 per cent. In the last patient it was necessary to use a vein graft (superficial femoral) to bridge a defect between the subclavian and pulmonary arteries. At autopsy a large embolus was found occluding the stenotic pulmonary artery and infundibulum. Unfortunately, the legs were not examined to determine whether the embolus originated at the site from which the vein graft was taken.

All other patients were 48 years of age or older (Table I).

Fourteen of the fatal embolisms occurred in women and 13 in men.

TABLE I. DISEASE, AGE, AND SITE OF OPERATION IN FATAL PULMONARY EMBOLISM (1946 TO 1949)

DISEASE	NUMBER	AGE (YR.)	OPERATION
Brain tumor	4	35, 48 58, 58	Craniotomy; partial removal
Carcinomatosis	2	54, 68	Liver and lymph node biopsy
Hip fracture	2	76, 85	Pin fixation; prophylactic superficial femoral vein ligation
Appendical abscess	2	53, 73	Appendectomy with drainage
Strangulated hernia	2	70, 73	Resection of ileum
Carcinoma of lung	2	52, 70	Pneumonectomy
Multiple lung abscess	2	55, 57	Pneumonectomy
Tic douloureux	1	50	Division V nerve
Carcinoma of prostate	1	72	Transurethral resection
Tetralogy of Fallot	1	14	Subclavian-pulmonary anastomosis with superficial femoral vein graft
Ventral hernia	1	63	Repair
Tuberculous meningitis	1	23	Ventriculogram
Diaphragmatic hernia	1	50	Repair, transabdominal
Total	22		

Activity of the Patients.—Since reliance was largely placed on early ambulation and bed exercises as prophylactic measures, the actual amount of activity of the patients in the fatal embolism group of 22 patients was carefully studied. Seventeen patients had not been out of bed following operation. Many of the bedfast patients were too ill to exercise. Two patients had been up in wheel chairs, 1 had been moderately ambulatory, and only 2 satisfied the criteria of full ambulation.

The Disease and Site of Operation.—Disease and site of the operations of the patients with fatal pulmonary embolism are shown in Table I. In most instances the patient's disease was a serious threat to life and many of the patients were seriously ill before operation. The risk of operation for nearly all patients was regarded as somewhat greater than usual.

The site of operation of patients dying of pulmonary embolism in the Hospital of the University of Pennsylvania from 1925 to 1945 is shown in Table II. In comparing Tables I and II, the differences in the categories listed are evident.

TABLE II. SITE OF OPERATION IN FATAL PULMONARY EMBOLISM (1925 TO 1945)

SITE	NUMBER
Bladder and prostate	11
Stomach	7
Inguinal and femoral hernia	6
Appendix	5
Leg (amputation)	5
Hip and leg (fracture)	5
Biliary tract	4
Rectum	3
Colon	3
Kidney	2
Pancreas	1
Abdomen (exploratory)	1
Spinal cord	1
Total	54

Premonitory Symptoms and Signs.—The clinical records were studied to determine whether any warning symptoms or signs existed prior to embolism. Since 1946, the legs of all patients undergoing major surgical procedures were examined at frequent intervals and any abnormalities were recorded. Temperature, pulse and respiration records, and laboratory reports were examined. In 14 patients no evidence could be found to indicate that a major thrombosis had occurred. In 4 patients fever and tachycardia, or a rising temperature and pulse, with a negative leg examination, preceded the embolism. In each instance these signs could have been, and were thought to be, accounted for by the patient's disease, the operative procedure, or another complication known to be present. Thus, in 18 patients (82 per cent) there was no clinical evidence of the occurrence of the thrombosis which preceeded fatal embolism. In 2 patients swelling of one leg had been noted but no active treatment instituted, while in the remaining 2, both comatose (craniotomies) and *in*

extremis for some time, swelling of one leg was apparently first noted by the pathologist at the autopsy table.

Site of Origin.—In 5 patients the site of origin of the embolus was not determined at post-mortem examination. In the 17 others the sites were as follows: femoral vein 8, iliac vein, 5, hypogastric vein 2, popliteal vein 1, and right auricle 1. The leg veins were not examined in the patient with thrombi in the right auricle and cannot be excluded as the source of the embolus. This patient was a 70-year-old woman with chronic auricular fibrillation.

Prophylaxis.—Specific prophylactic measures, other than those listed under General in Chart 1, were employed in only 2 patients. Bilateral superficial femoral vein ligation was performed in both patients. Both had hip fractures. One a woman 76 years of age, had a fatal embolus on the fourteenth day after the hip fracture was pinned and the other, a man 85 years of age, had a fatal embolus on the fifteenth day after pinning. In both instances the embolus was found to have arisen from a thrombus which formed above the site of ligation.

Duration of Life After Embolism.—In most instances the embolism was massive enough to cause death within fifteen minutes, despite emergency treatment. Only 2 patients lived for more than one hour: 1 for eleven, and one for eighteen hours. In these instances the patients did not respond to treatment and remained in shock until death.

NONFATAL PULMONARY INFARCT

Twenty-four patients were considered on the basis of chest pain, cough, hemoptysis, x-ray examination, electrocardiographic tracings, and clinical course to have nonfatal pulmonary infarcts. In only 3 were there dyspnea, cyanosis, and prostration.

Age and Sex.—Six patients were under the age of 40 years and, in general, the ages were lower than in the fatal embolism group (Table III). Non-

TABLE III. DISEASE, AGE, AND SITE OF OPERATION IN NONFATAL PULMONARY INFARCT (1946 TO 1949)

DISEASE	NUMBER	AGE (YR.)	OPERATION
Cancer of rectum	2	45, 54	Abdominoperineal resection
Cancer of colon	2	67, 74	Resection
Fracture of hip	2	60, 83	Internal fixation
Appendicitis	2	33, 33	Appendectomy
Benign prostatic hypertrophy	2	65, 67	Suprapubic prostatectomy
Cholelithiasis	2	40, 49	Cholecystectomy
Duodenal ulcer	1	53	Gastrectomy
Spinal cord tumor	1	52	Laminectomy
Traumatic finger amputation	1	33	Tubed abdominal flap
Varicose veins	1	36	Excision
Cancer of tongue	1	74	Radical neck dissection
Ulcerative colitis	1	50	Ileostomy
Arteriosclerotic gangrene	1	68	Supracondylar amputation
Essential hypertension	1	40	Smithwick
Popliteal arteriovenous fistula	1	47	Excision
Cyst of pancreas	1	47	Excision
Calcified empyema	1	38	Preoperative
Thrombophlebitis	1	30	Preoperative
Total	24		

fatal infarcts occurred predominately in men, the ratio being 17 men to 7 women.

Activity of Patients.—The patients in this group were more active than in the fatal embolism group. Only 7 had not been out of bed since operation. Nine were moderately ambulatory, and the remaining 8 were fully ambulatory.

The Disease and Site of Operation.—Disease and the site of operations were more varied than in the fatal embolism group and there was little correlation between these factors in the two groups, as is seen in Tables I and III.

Premonitory Symptoms and Signs.—Evidence that embolization was about to occur was no more apparent than in patients with fatal pulmonary embolism. In 14 there were neither warning symptoms or signs, while in 7 the occurrence of fever and tachycardia, in the absence of leg signs, was considered to be due to other causes already diagnosed. In the remaining 3 patients there was evidence of phlebitis of the legs prior to infarction.

Treatment.—In all patients active treatment was instituted as soon as possible after the infarction occurred. The treatment used was as follows: ligation alone, 10; ligation plus anticoagulants, 8; anticoagulants alone, 6. In 3 patients additional infarcts were diagnosed following ligation and anticoagulants were employed for this reason.

POSTOPERATIVE PHLEBOTHROMBOSIS AND THROMBOPHLEBITIS

Seventy-six patients developed phlebothrombosis or thrombophlebitis in the lower extremities during the three-year period, an incidence of 0.44 per cent (1 in 225 operations). None showed evidence of pulmonary infarction. In 17 patients (22 per cent) the disease was confined to the saphenous system, and in the majority it was thought to be initiated by a phlebotomy performed at operation. No complications developed in any of these patients. Anticoagulant therapy was used in 2, with rapid improvement of symptoms. Ligation was not performed in any. Fifty-nine (78 per cent) developed signs of deep vein thrombosis. Eighty per cent of the patients with deep vein thrombosis were over 40 years of age, in contrast to only 30 per cent with saphenous thrombosis.

Seventy-two per cent of the patients with deep vein thrombosis were treated by ligating the superficial femoral vein bilaterally. Clots were found in the vein at operation in 4, who were subsequently treated with anticoagulants. Twenty-seven per cent of the patients with deep vein thrombosis were treated with anticoagulants alone.

COMMENT

It is evident that the antiembolic measures employed during the past three years have not reduced the incidence of fatal pulmonary embolism, particularly in elderly patients who must be confined to bed because of a severe operation and illness. A comparison of the site of operation during the past

three years (Table I) and the preceeding twenty-five years (Table II) suggests that early ambulation and greater attention to general prophylactic measures may have reduced the incidence of fatal embolism in patients undergoing major procedures which were done commonly in both groups, that is, operations on the stomach, biliary tract, colon, rectum, prostate, and bladder.

The absence of pulmonary infarction in 59 patients with deep vein thrombosis, and of subsequent fatal embolism in 24 patients with nonfatal pulmonary infarction, suggests that the use of proximal vein ligation and anticoagulants in these patients effectively prevented further complications. Without using these methods, nonfatal pulmonary infarction was found to occur in one-third of the patients with thrombophlebitis,[2] and fatal pulmonary embolism in one-fifth of the patients with previous nonfatal pulmonary infarction.[3]

The finding of Evans and Dee[4] that warning symptoms and signs were present in 85 per cent of their patients before fatal embolism occurred has, unfortunately, not been confirmed in our experience. Between 1941 and 1946, there was no warning in 71 per cent,[1] and in the present series, 1946 to 1949, there was no warning in 82 per cent. In 1946 it was hoped that more frequent and more careful examinations of the legs might reveal a higher incidence of warning signs. This has not proved to be true. The occurrence of fatal embolism without warning in most instances has also been the experience of Allen.[5]

Since there is usually no warning, deaths from pulmonary embolism must be prevented in one of two ways: (1) by the use of an effective method of mass prophylaxis; or (2) by the use of a laboratory test which will detect the imminence or the presence of thrombosis while there is still time for adequate protective treatment.

The methods of mass prophylaxis which offer encouragement are early ambulation, anticoagulation, and proximal vein ligation. Early ambulation, as stated previously, may have been helpful in reducing the incidence of fatal embolism in our patients who underwent major operations and were able to undertake active postoperative walking on the day of operation or the first postoperative day. Since only 3 patients with fatal embolism were ambulatory this method was not applicable in patients who had embolic deaths. The physiologic basis and the results of early ambulation throughout the world have been discussed in the recent book of Leithauser.[6] We realize that subsequent studies may not substantiate all of Leithauser's conclusions.

Prophylactic superficial femoral vein ligation has been studied extensively by Allen[5] and his associates, who have reported its use in 984 elderly patients in whom the risk of fatal embolism was known, from previous experience, to be unusually great. Four patients died of pulmonary embolism. In 2 the emboli originated in the iliac and in 2 in the deep femoral veins. In a "control" series of 984 patients of similar sex, age, and lesion, 37 patients died of pulmonary embolism. By the use of this prophylactic method, therefore, 33 deaths from pulmonary embolism were apparently prevented. During 1946 and 1947 a considerable number of prophylactic ligations were done on our

service. Enthusiasm for this procedure was dampened, however, by the occurrence in October, 1947, of 2 deaths from embolism following prophylactic ligation. Erb and Schumann[7] were similarly discouraged by their experience with prophylactic ligation at the Philadelphia General Hospital. In a series of 100 consecutive patients with hip fractures, bilateral, superficial, femoral ligation was done in alternate patients. Death from massive pulmonary embolism occurred in 2 of the 50 ligated patients and in 2 of the 50 not ligated. In addition, nonfatal pulmonary infarction occurred in 7 patients following ligation and in 4 who were not ligated.

The prophylactic use of heparin was begun as early as 1937 by Crafoord,[8] and in 1941 he[9] reported the results in 325 patients, in whom the incidence of thromboembolic complications was greatly reduced. Others have since studied large series in which prophylactic anticoagulants were used and in recent reports there is impressive statistical evidence of protective action against fatal embolism by both heparin[10] and Dicumarol.[11-13] This protection has been obtained at the risk of hemorrhage and in some instances fatal hemorrhage has occurred.[11, 13] Up to the present time our experience with prophylactic anticoagulants has been limited because of the lack of adequate technical assistance and the recognition that the merit of the method was being studied by competent investigators elsewhere. Recent experimental studies in our laboratory suggest that it is not necessary to reduce the prothrombin percentage to hemorrhagic levels in order to obtain protection against thrombosis by Dicumarol therapy.[14]

Because of the frequent absence of clinical signs of thrombosis, and the unreliability of the usual tests of the clotting mechanism in demonstrating increased coagulability of the blood, a laboratory test sufficiently sensitive to detect incipient or actual subclinical thrombosis has been sought. The heparin tolerance test of de Takats[15] and the modified prothrombin test of Brambel and Loker[16] have been proposed for this purpose, and extensive clinical studies of their reliability are in progress. More recently Sandrock and Mahoney[17] have reported encouraging results in determining the prothrombin activity of postoperative patients, although full confirmation of their results was not obtained by others.[18] Within the past year Kay and Ochsner[19] have proposed a new test in which the prothrombin and antithrombin levels are followed daily during the postoperative period. Although their series is not large, the data at present suggest that the danger of thrombosis may be reliably demonstrated, and that the administration of alpha tocopherol pre- and postoperatively to increase antithrombin activity may prevent postoperative thrombosis and embolism.

CONCLUSIONS

1. An analysis of thromboembolic complications at the Hospital of the University of Pennsylvania during the past three years showed that the incidence of fatal pulmonary embolism was not reduced by a regimen of prophylaxis and treatment instituted in 1946.

2. In 82 per cent of patients with fatal pulmonary embolism no clinical signs of thrombosis were apparent prior to embolism.

3. It is probable that the incidence of fatal pulmonary embolism can be reduced only by effective mass prophylactic measures or the development of a laboratory test which demonstrates incipient thrombosis.

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TREATMENT OF EXPERIMENTAL ACUTE ARTERIAL INSUFFICIENCY

A Comparison of the Sympatholytic Agent Priscoline* (2-Benzyl-4,5-Imidazoline HCl) and Sympathectomy

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PRISCOLINE (2-benzyl-4,5-imidazoline HCl) is a sympatholytic and adrenolytic agent which has been given extensive experimental and clinical trial in hypertension,[1, 2] organic arterial insufficiency,[1-6] inorganic (vasospastic) arterial insufficiency,[7-9] and the vascular insufficiencies resulting from exposure to cold.[10]

The chemistry and pharmacologic actions of Priscoline have been studied by numerous investigators, both here and abroad.[11-22] The site of action is the smooth muscle termination of sympathetic postganglionic fibers, although there is evidence suggesting an additional, local, histamine-like effect.[2] The most striking action of the drug is a generalized vasodilatation with coincident fall in systemic blood pressure levels.[11, 13, 14, 18] However, Priscoline increases cardiac output, and in some cases this increase is sufficient to overcome the hypotension resulting from generalized peripheral vasodilatation, in which event elevation of the blood pressure will occur.[19] The vasopressor effect of Adrenalin (epinephrine) is abolished or reversed,[13, 17, 18, 19] although the pupillary reaction (mydriasis) remains unchanged following administration of Priscoline.[18] Priscoline stimulates the ileum in the dog, a cholinergic action which may be blocked by atropine.[20]

The study reported here is a comparison of Priscoline and sympathectomy, the latter a procedure of known experimental and clinical value in acute arterial insufficiency.[23-31] In addition to survival and rehabilitation, blood flow to the ischemic limb was studied by instrumental methods.

METHOD

The experimental animals used in this study were healthy, adult, mongrel dogs. Circulation to the hind extremities was reduced to critical levels by excision of the aortic trifurcation, and concomitant ligation of the paired deep circumflex iliac arteries. Sterile technique was used in all operative procedures.

The instrumental study included plethysmography, skin and muscle temperatures, and the removal of radioactive sodium. These determinations, with the exception of radioactive sodium (Na^{24}) removal, were made preoperatively, immediately postoperatively, and on the first, third, and fifth postoperative days. The relatively short half-life of the radioactive sodium (14.8 hours)

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made it impossible to carry out mobilization studies at the same time intervals used in the other determinations. The isotopic studies were made preoperatively, immediately postoperatively, one day postoperatively, and in cases of survival seven days postoperatively. It was necessary to administer general anesthesia for the performance of these tests, a factor of importance to be discussed subsequently. The anesthetic used was Nembutal (pentobarbital sodium), 64 mg. per 2.2 kg. body weight, administered intravenously.

Ten control and ten Priscoline-treated dogs were subjected to operation and the tests just enumerated. In the treated animals, intramuscular injections of Priscoline, 5 mg. per kilogram were given at the conclusion of the operative procedure, repeated every four hours for two doses, and then continued at eight-hour intervals throughout the first five postoperative days. The smallest dose of Priscoline consistent with sympatholysis was given to avoid significant degrees of hypotension. All injections were made in the triceps muscle of the foreleg. An additional ten dogs were subjected to bilateral lumbar sympathectomy immediately following aortic excision.

OPERATIVE PROCEDURES

Aortic Excision.—The abdomen was opened through a left rectus, muscle-splitting incision and the posterior peritoneum overlying the aortic trifurcation incised. The deep circumflex iliac arteries were divided between ligatures, and the lowermost portion of the aorta and its three terminal branches (that is, the right external iliac, left external iliac, and common hypogastric arteries) were excised. The posterior peritoneum was joined and the abdomen closed in layers.

Sympathectomy.—Following excision of the aorta, the left lumbar sympathetic chain was identified lying anterolateral to the vertebral bodies. It was dissected superiorly and divided at the level of the first or second lumbar ganglion. The chain was excised inferiorly to the level of the seventh lumbar ganglion. A similar procedure was performed on the right, the chain being dissected from its position beneath the inferior vena cava. The posterior peritoneum was approximated and the abdomen closed in layers. The sympathetic chains were examined microscopically and the presence of ganglion cells was established. Postoperative roentgenograms showing dural clips at the points of division of the chain identified the exact levels of sympathectomy in each dog.

TESTS

Plethysmography.—Total blood flow to one of the posterior extremities (right) was measured by the venous occlusion air plethysmograph. The instrument used in this laboratory is an adaptation of that originally described by Eckstein and associates.[32] The procedure is based on the principle that following sudden occlusion of venous return the extremity will swell, the increase in volume resulting from arterial inflow. The air plethysmograph is designed to measure the initial rate of increase in volume following venous occlusion and to record the volume changes optically. Permanent photographic

records are obtained from which arterial flow to the extremity may be calculated as cubic centimeters of blood entering the leg per minute per 100 c.c. of leg volume.

Plethysmography yielded information regarding flow to all tissues of the extremity, in contrast to skin and muscle temperature values and radioactive sodium mobilization. The latter methods evaluate blood flow to skin and muscle only.

Skin Temperature.—Fahrenheit readings over the thigh, knee, calf, and both surfaces of the foot were made with a thermocouple. Room temperature was regulated so that all measurements were made within a 1 to 2° variation in environmental temperature (78° F.).

Muscle Temperature.—Temperature readings (Fahrenheit) were made in the gracilis and gastrocnemius muscles using a thermocouple and a standard potentiometer.

Radioactive Sodium Mobilization.—The rate of removal of Na^{24} from muscle is dependent upon the adequacy of the circulation to the muscle.[33, 34] Removal values were obtained by injecting Na^{24} into the gastrocnemius muscle (right leg) overlying a Geiger-Mueller counter. The percentage of injected Na^{24} which was removed in a ten-minute interval was determined by the use of electromechanical apparatus. This percentage was designated "removal factor."

RESULTS

It has been reported that aortic excision and division of the deep circumflex iliac arteries result in a mortality rate of 90 to 100 per cent.[35, 36] Following this procedure the posterior extremities become cold, cyanotic, edematous, and paralyzed. Death follows in three to four days.

Figs. 1 and 2 are composite graphs showing results in the control, Priscoline-treated, and sympathectomized animals.

Control Group.—Four animals survived the critical period and regained function to a significant degree. One week postoperatively three of these four animals were using their hind legs, although requiring frequent rest periods. The fourth animal exhibited a unilateral foot drop two months postoperatively. Five animals succumbed to gas bacillus infection; all died on or before the fourth postoperative day. One dog survived ten days and developed dry gangrene of both hind feet.

Priscoline-Treated Group.—One animal survived the critical period, regaining complete use of the hind extremities. Six animals died of gas bacillus infection on or before the fourth postoperative day. Three animals developed dry gangrene of one or both hind feet and died on the sixth, seventh, and eighth postoperative days. Prior to death, return of function in the Priscoline-treated dogs was uniformly poorer than in the control group.

Sympathectomized Group.—Five animals survived the critical period, all regaining adequate function. There was one death from gas bacillus infection

on the second postoperative day and two deaths from the same cause on the third postoperative day. Two animals died of dry gangrene on the seventh and seventeenth postoperative days.

Death in all groups resulted from either gas bacillus infection or dry gangrene. These animals exhibited the cold, paralyzed hind extremities characteristic of profound ischemia. The dogs dying of *Clostridium welchii* infection exhibited minimal swelling and crepitus approximately twenty-four hours after operation, the infection progressing rapidly to fatal termination within two to four days. In the great majority of instances, the gas bacillus infection was most extensive in the left thigh.

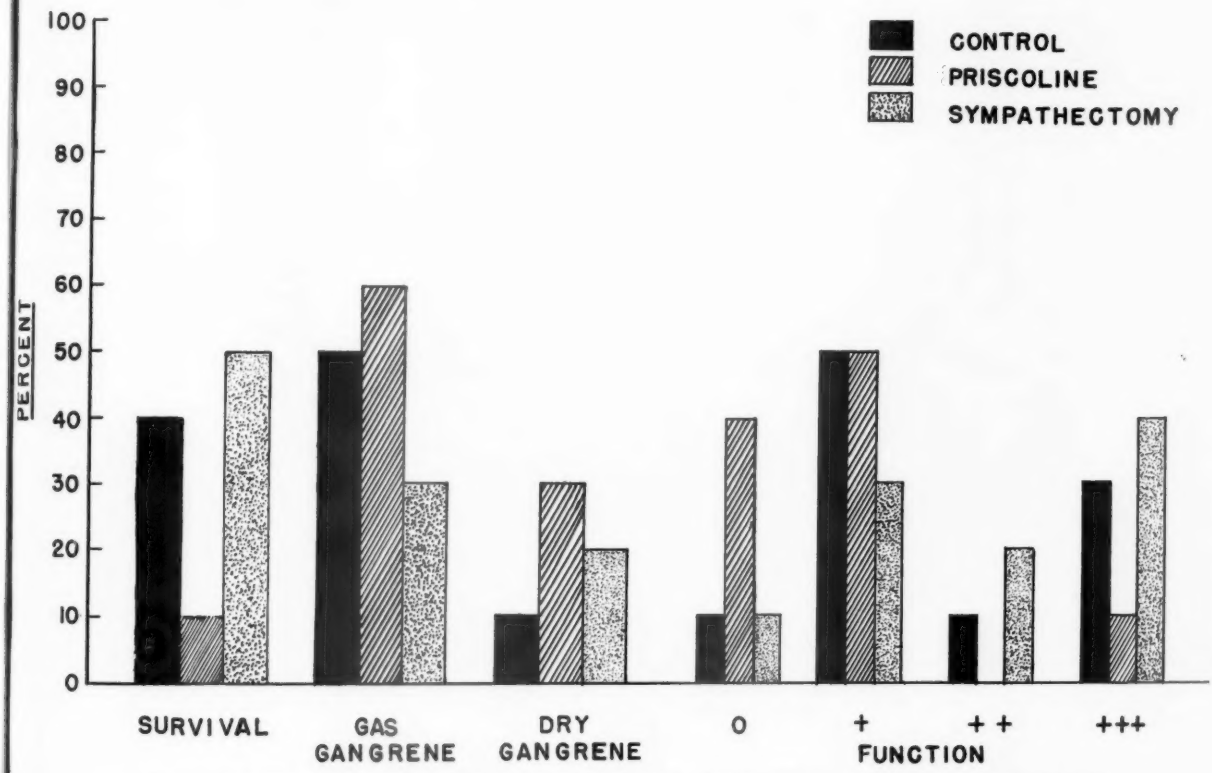

Fig. 1.—Composite chart showing survival rate, incidence of gas and dry gangrene, and evaluation of function (0 represents total paralysis with inability to raise hind extremities from the floor; +++ indicates complete return of function of hind extremities without obvious stigmata of vascular insufficiency, that is, trophic ulcers, cyanosis, muscle tremor, foot drop, or apparent claudication).

Dry gangrene was noted on the fifth to tenth postoperative days and death followed in two to seven days. Necrosis began at the nail beds and encompassed approximately one-half the foot. On occasion, gangrenous areas were noted on the legs. There was no predilection for right or left foot in any of the three groups.

Function was evaluated as explained in Fig. 2. The sympathectomized animals exhibited a greater return of function in the survivals and less diminution of function in the casualties than either of the other two groups.

Comparison of Total Blood Flow.—There was little difference in total blood flow throughout the first five days in the control and sympathectomized groups.

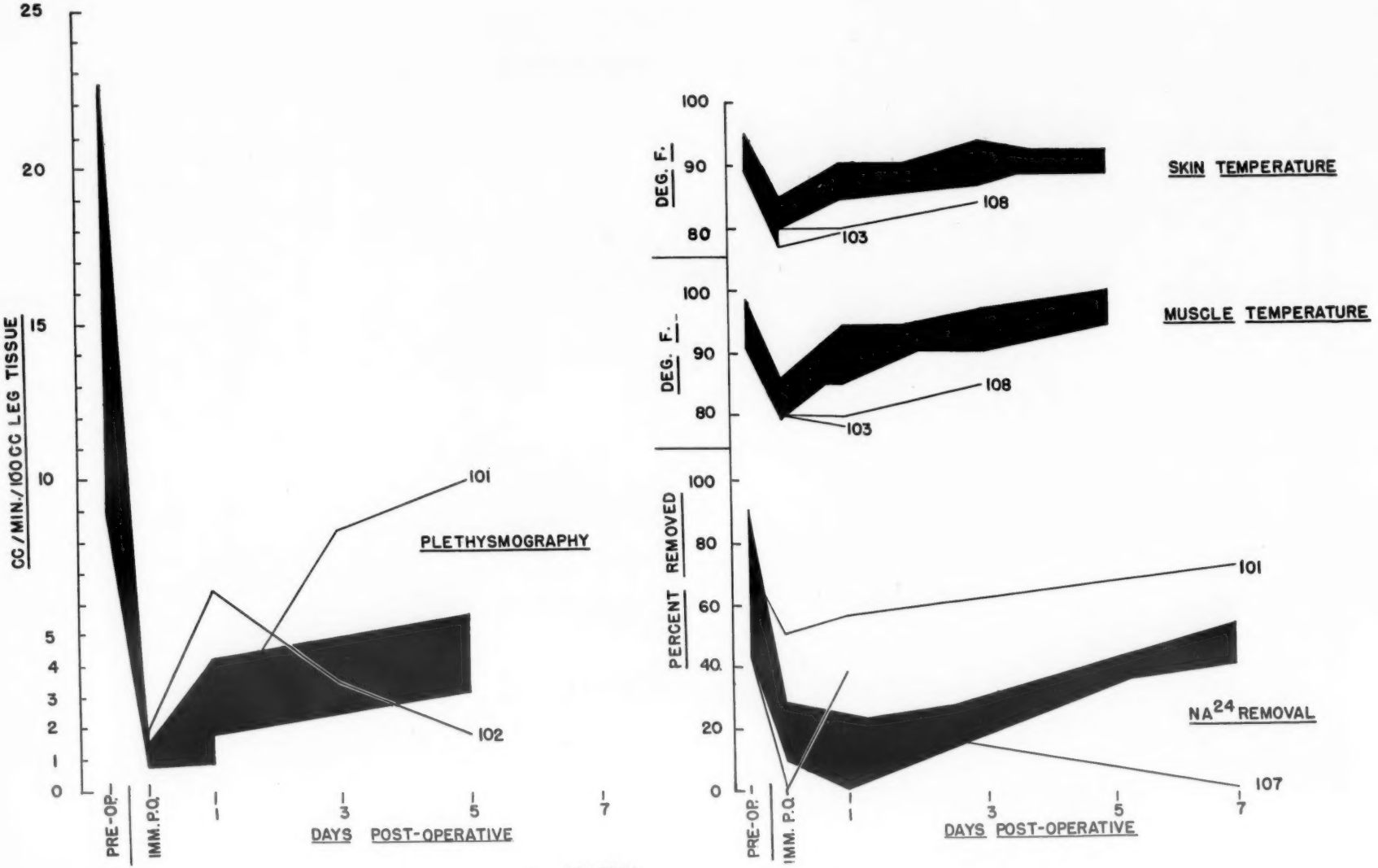

Fig. 2.—Composite graph showing blood flow (cubic centimeters per minute per 100 c.c. of leg volume), temperature of skin overlying gastrocnemius muscle, gastrocnemius muscle temperature, and radioactive sodium removal from the gastrocnemius muscle (per cent of amount injected which was removed in ten minutes), in the control (*A*), Priscoline-treated (*B*), and sympathectomized (*C*) animals. The numbers in the graph refer to individual dogs.

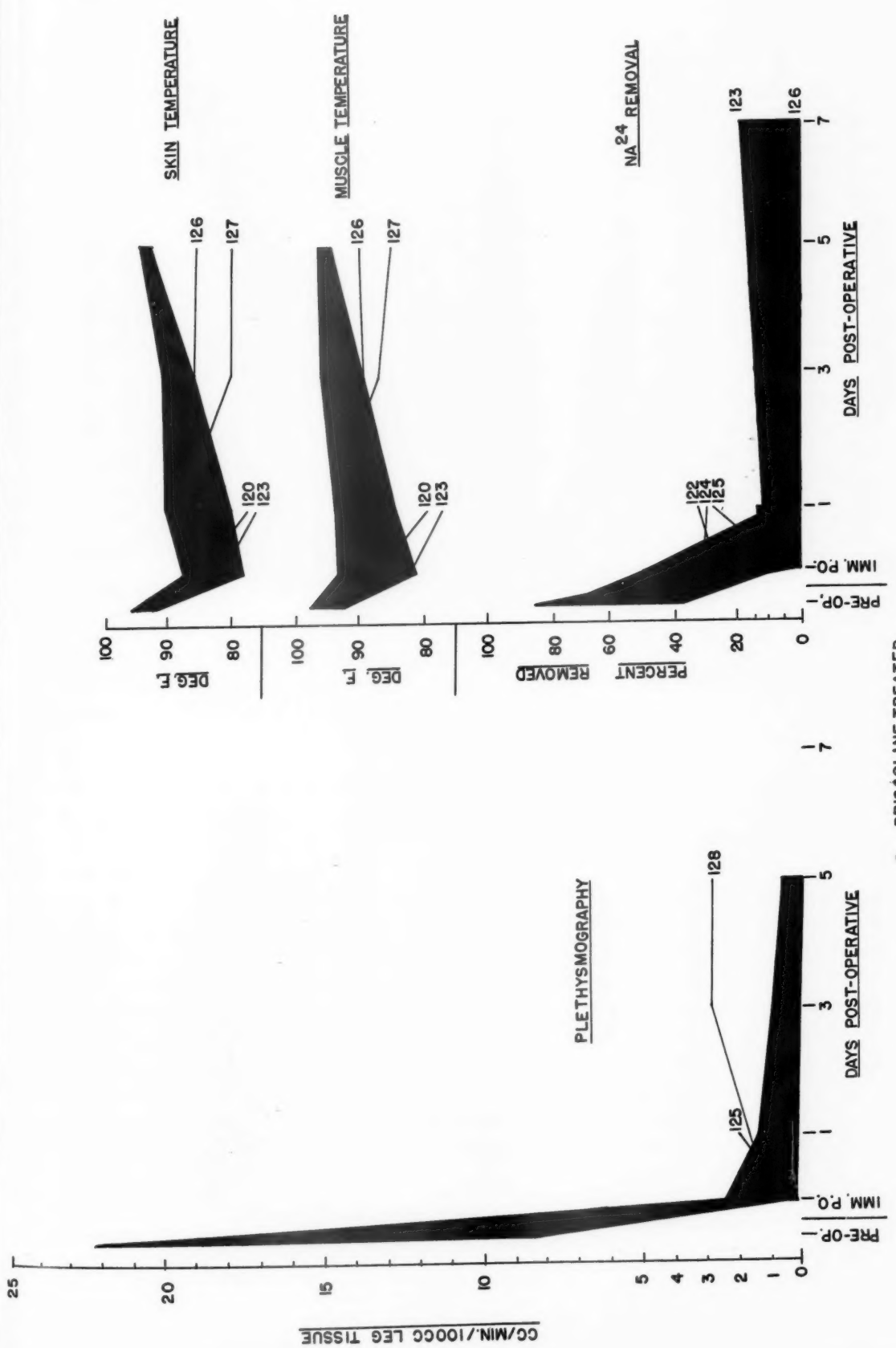

Fig. 2.—(*Continued.*)

muscle, gastrocnemius muscle temperature, and radioactive sodium removal from the gastrocnemius muscle (per cent of amount injected which was removed in ten minutes), in the control (*A*), Priscoline-treated (*B*), and sympathectomized (*C*) animals. The numbers in the graph refer to individual dogs.

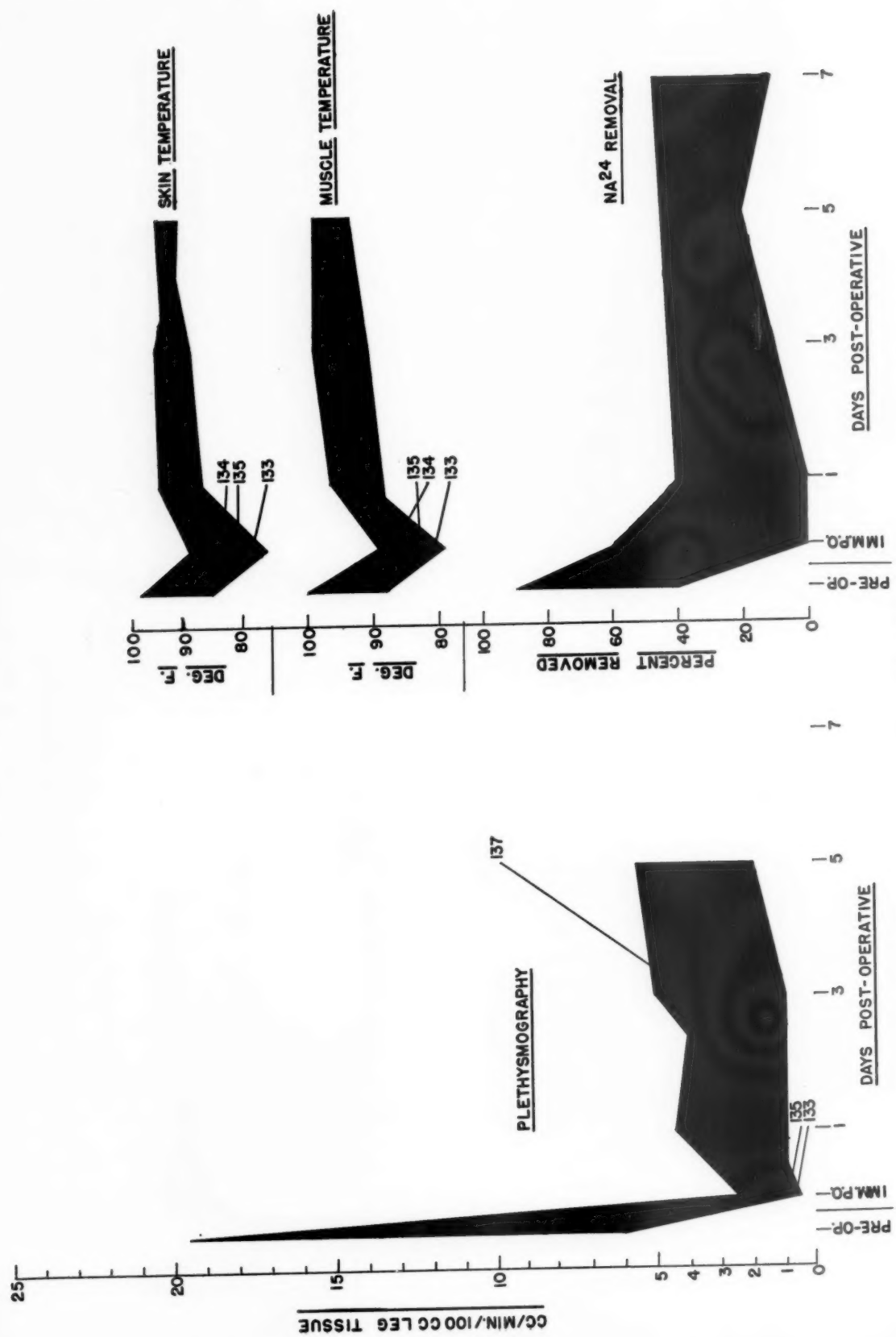

Fig. 2.—(*Concluded.*)

The range was between 2 to 5.3 c.c., except in a single dog in each group, in which there was a large flow at the end of the study period. Blood flow in the Priscoline-treated dogs continued to fall throughout the postoperative period; of those animals surviving, at five days only one had a flow greater than 0.6 c.c.

Comparison of Skin Temperature.—A comparison of average skin temperature readings revealed that the sympathectomized dogs maintained somewhat higher values than the control series (2.2° F. on the first postoperative day, 2.8° F. on the third postoperative day, and 0.9° F. on the fifth postoperative day). At the conclusion of five days the average skin temperature reading of the sympathectomized dogs had returned to within 2.2° F. of the preoperative level (94.2° F.). Average skin temperature in the Priscoline-treated group was as much as 5.5° F. lower than the sympathectomized dogs, and 2.3° F. lower than the controls.

Comparison of Muscle Temperature.—Muscle (gastrocnemius) temperatures in the control and sympathectomized groups paralleled the skin temperatures at a higher level throughout the postoperative period, although at the fifth postoperative day there was no longer a gradient in average temperature between the two groups. On the fifth day the average muscle temperature of the Priscoline-treated dogs was 5.3° F. lower than the other groups.

Comparison of Radioactive Sodium Mobilization.—The Na^{24} removal values in the control and sympathectomized groups were approximately the same, and there was no significant difference as had been noted in the skin and muscle temperature studies. In contrast, Na^{24} studies made on the seventh postoperative day on the Priscoline-treated animals showed the low values indicative of a less adequate muscle blood flow.

Fig. 2.—(*Concluded.*)

DISCUSSION

The survival rate with return of adequate function in the control group was higher than that previously reported.[35, 36] These results are probaly attributable to the repeated administration of pentobarbital sodium in anesthetic amounts.*

Although the question of a specific sympatholytic action of the barbiturates is unsettled, it is known that barbiturate-induced general anesthesia has a depressant action upon the proprioceptive mechanism for regulation of vasomotor tone (that is, pressoreceptor vasomotor reflexes originating from the carotid sinus, aortic arch, vena cava, and pulmonary artery).[37] Intraperitoneal Nembutal has also been reported to have prevented the marked fall in skin temperature usually seen following ligation of the dog's femoral artery.[38] It appears that Nembutal, in anesthetic dosage, is a vasodilating agent; the vasodilating effect apparently results from a depression of the peripheral proprioceptive receptors, the central vasoconstrictor centers in the floor of the fourth ventricle, and the subsidiary vasoconstrictor centers in the thoracolumbar region of the spinal cord.

*Five additional dogs were subjected to excision of the aortic trifurcation and ligation of the deep circumflex iliac arteries. These animals received general anesthesia only once, in contrast to the groups which received repeated injections of pentobarbital sodium throughout the first five postoperative days. In this series, one animal survived with adequate return of function. Three animals died of massive gas bacillus infection, and one of dry gangrene.

In the present study, the period of general anesthesia resulting in a diminution or abolition of vasomotor tone with secondary vasodilatation was of limited duration (two to five hours). Therefore, the animal was subjected to intermittent periods of generalized vasodilatation throughout the postoperative period.

The low survival rate, poor function, and instrumental evidence of totally inadequate blood flow in the Priscoline-treated group is significant.* A possible explanation of these results is to be found in the "borrowing-lending" hemodynamic phenomenon (hemometakinesia) postulated by DeBakey and co-workers.[39] As a result of a relatively fixed total blood volume, increased blood flow to an extremity occurs only through redistribution of this total volume. The acquisition of an augmented blood flow by one portion of the body is made possible by the reduction of vascular bed volume in other regions.

The generalized vasodilatation produced by Priscoline inhibits the process of hemometakinesia by blocking the nerves through which reduction in the vascular bed volume is mediated. In the Priscoline-treated animal, therefore, the total blood volume cannot be readjusted to allow an increase in the blood supply to the posterior extremities.

These results appear to be in agreement with the view of DeBakey and associates,[39] Smithwick,[40] and Martin and associates,[41] who feel that generalized vasodilating agents are of no value in significantly increasing circulation to an ischemic portion of the body. It appears that Priscoline, when administered in sympatholytic dosage to experimental animals suffering from profound arterial insufficiency, not only is ineffectual, but is actually deleterious.

Sympathectomy was of limited value in this study. Although there was little difference in survival rate between sympathectomized and control groups, function was uniformly better in the former series. The sympathectomized animals also exhibited higher skin and muscle temperatures during the postoperative period. In noting the relatively low survival rate in the sympathectomized dogs, it must be remembered that circulation to the hind extremities was reduced to an absolute minimum through the division of the deep circumflex iliac vessels in conjunction with aortic excision. The deep circumflex iliac arteries are the last large vessels to arise from the aorta before its division, and are a major source of collateral supply to the hind extremities. Leriche has reported 100 per cent survival in animals subjected to aortic excision and bilateral lumbar sympathectomy.[42, 43] However, the sympathectomy was performed at a preceding operation and the deep circumflex iliac arteries were not interrupted at the time of aortic excision. It is felt that these significant differences account for the failure to reproduce results comparable to those of Leriche.

*To preclude the possibility of the sympatholytic effect of Priscoline being activated by Nembutal in the Priscoline-treated series, an additional ten dogs were subjected to aortic excision and division of the deep circumflex iliac arteries without subsequent anesthesia during the first seven postoperative days. Priscoline, 5 mg. per kilogram, was given exactly as in the former series. Five animals in this group died within three days with *Cl. welchii* infection and three animals developed dry gangrene. Function in the two surviving dogs was 2 plus and 3 plus.

SUMMARY

A group of thirty dogs was subjected to excision of the aortic trifurcation and division of the deep circumflex iliac arteries for the purpose of comparing the new sympatholytic agent Priscoline with actual sympathectomy in the treatment of acute arterial insufficiency. The effect of therapy was evaluated clinically as well as by means of instrumental methods, including venous occlusion plethysmography, skin and muscle temperature measurements, and the mobilization of intramuscularly injected radioactive sodium.

The survival of an ischemic extremity is dependent upon the interaction of the following factors: (1) Maximal dilatation of collateral blood vessels and, (2) adequate distribution of total blood volume to enable filling of the collateral vessels.

The results obtained in this study suggest that *intermittent generalized vasodilatation*, induced by agents acting centrally or peripherally, is of definite value. The abolition of normal or increased vasomotor tone resulting from the operative manipulation of the aorta and iliac vessels allows maximum dilatation of existing collateral channels, following which the normal neural regulatory mechanism is restored. As a result of the dilatation, a greater volume of blood is distributed to the posterior extremities. Conversely, administration of Priscoline in a dosage designed to produce constant sympatholysis was unsuccessful, for although vasomotor tone was obliterated and collateral vessels dilated, the vasomotor mechanism necessary for the distribution of blood to these vessels was inhibited. It is believed that the therapeutic efficiency of the sympatholytic drugs may be greatly enhanced if the drugs are administered so as to produce an intermittent rather than a constant vasodilatation and reduction of vasomotor tone.

CONCLUSIONS

1. Continuous, Priscoline-induced sympatholysis is ineffective in the treatment of experimental, acute arterial insufficiency.

The generalized sympathetic blockade produced by Priscoline inhibits the neural regulatory mechanism responsible for redistribution of blood volume.

2. The production of localized vasodilatation by means of lumbar sympathectomy was of value in this study, although limited by the severity of the vascular insult.

Collateral dilatation without sacrifice of the normal vasomotor regulatory mechanism makes sympathectomy a more rational procedure in the treatment of acute arterial insufficiency.

3. The administration of vasodilating agents in a dosage designed to produce intermittent, rather than constant, vasodilatation may increase their therapeutic value in acute arterial insufficiency.

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STUDIES ON CARCINOMA OF THE LARYNX

A Method of Exteriorization of the Larynx in the Dog

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THE larynx of the anesthetized dog is readily visualized by simply lifting the epiglottis out of the way with forceps or by direct laryngoscopy. However, a more direct method of inspection at periodic intervals is feasible in the intact and unanesthetized animal. As repeated observation of any structure is necessary either to study the possible action of systemic drugs and hormones on the organ or to investigate the effect of repeated direct local application of certain drugs and irritants, the following operation was devised as a method for studies of the larynx in the dog.

PROCEDURE

Under Nembutal anesthesia the dog is placed in a supine position with head extended. An endotracheal tube is introduced through the mouth and the larynx into the upper trachea. The anterior neck is shaved from the mandible to the sternal notch. This area is prepared and draped.

A 6 cm. vertical midline incision is made beginning at a point 1 cm. above the hyoid bone. The incision is carried through the platysma muscle and lateral flaps are elevated for a short distance in this plane. The hyoid bone is immediately identified in the upper portion of the incision, and the insertions on the hyoid of the sternohyoid, thyrohyoid, and omohyoid muscles below, the digastric muscles above and lateral, and the mylohyoid and geniohyoid muscles above are divided. It is now possible to separate the hyoid from the intrinsic muscle of the tongue and remove it completely. This does not injure either the superior laryngeal vessels or nerves.

The pre-epiglottic space is now exposed in the midline of the incision in the area previously occupied by the ccentral portion of the hyoid bone. Submucosal dissection is carried upward on the anterior surface of the epiglottis until the pharynx is finally entered at its tip. This tip of the epiglottis is grasped with a tenaculum and the mucous membrane carefully incised along both right and left borders of epiglottis and aryepiglottic folds as far back as the arytenoids.

At this point the intratracheal tube is withdrawn from the mouth. Usually it is not necessary to reinsert a similar tube through the wound directly into the larynx and trachea provided the airway is carefully protected and in no way impinged upon during the remainder of the operation.

The mucous membrane is now undermined behind the arytenoid and cuneiform cartilages on both sides in the line where the mucous membrane of the upper anterior esophagus becomes continuous with the posterior surface of the larynx. When this has been incised it is possible to elevate the larynx and

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completely free it from anterior esophageal wall for a distance of 3 cm. or more. The larynx has now been completely separated from the pharynx, hypopharynx, base of tongue, and the esophagus. The resultant opening in anterior pharyngeal wall is closed longitudinally with a double row of interrupted mattressed silk sutures. After the mucous membrane has been sutured, strap muscles are approximated in the midline to reinforce the suture line in the pharynx.

It is now possible to estimate the exact length of the epiglottis. A skin flap of suitable size is outlined on each side of the previous skin incision. These flaps are to be joined in the midline to cover the anterior surface of the epiglottis. The flap on each side is pointed at its apex and about 2 cm. in width at its base. After each has been elevated in the plane of the platysma, it is sutured to its partner in the midline. Their free lateral borders are now sutured with interrupted silk sutures to the mucous membrane of the epiglottis. The upper portion of the midline incision is now approximated in the midline and the small remaining defect closed by suturing the mucous membrane of aryepiglottic folds and the posterior laryngeal region to the skin.

The larynx (and airway) is now completely freed from the pharynx or from any communication with the gastrointestinal tract (see Figs. 1 and 2). None of the nerves or blood vessels to the larynx have been severed. There are no raw areas remaining on the neck. The dog has an adequate airway and can eat normally.

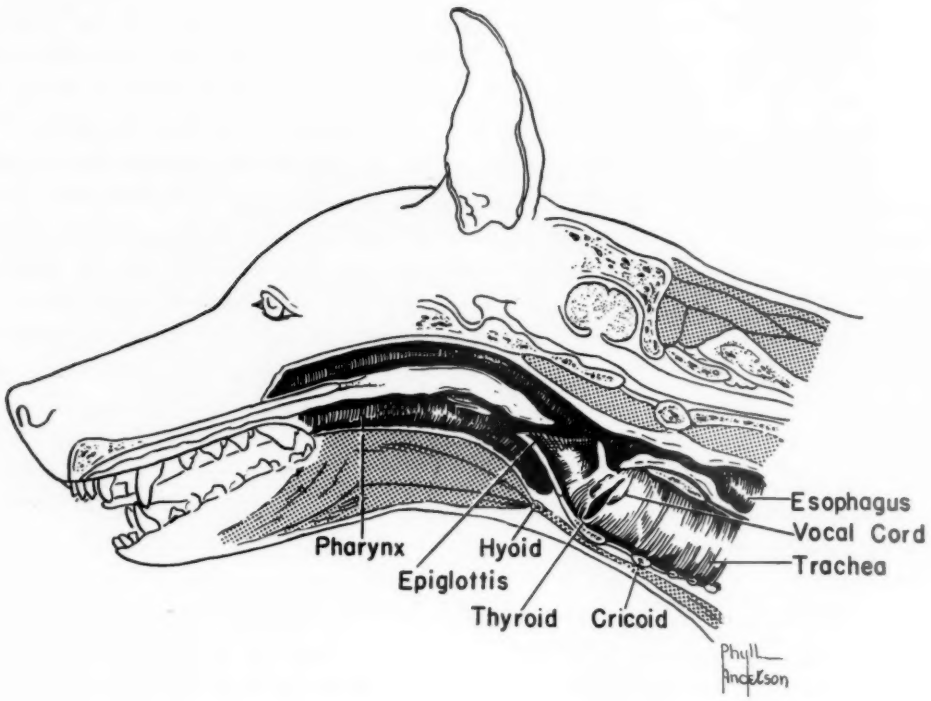
As the dog has been under general anesthesia it is necessary to safeguard his airway during the period of recovery. For this reason a mental frame is applied along the spine to keep neck and head extended (see Fig. 3). This begins at the mid-portion of the trunk and extends beyond the ears. The posterior portion of the frame is held by a harness which extends beneath the mandible at the angle of the jaw. This must be securely fastened. The dog can eat with the harness in place. At the same time it prevents his flexing the neck and producing asphyxia during the period of recovery. This harness has been allowed to remain in place at least forty-eight hours.

The dogs are allowed to take liquids as soon as they desire and are rapidly encouraged to take a soft diet. Except in those instances in which a pharyngeal fistula has occurred during period of healing, there has been no difficulty with postoperative care. However, a pharyngeal fistula is quite common, due primarily to the dog's own actions in that he may try to scratch the exposed pharynx on the underside of the neck with the hind foot. As soon as the dog becomes acclimated to the presence of the larynx in this area it does not seem detrimental or annoying to him.

DISCUSSION

This procedure is a relatively simple surgical procedure. The difficulties encountered in developing it were due to minor points which were corrected in successive stages. The procedure is well tolerated by the dogs after full healing has occurred. The dogs bark in the usual fashion although the voice comes from the underside of the neck. There is no apparent difficulty with the aspiration of foreign material. There has been no interference with swallowing related to the reconstruction of the pharynx and esophagus.

Fig. 1.



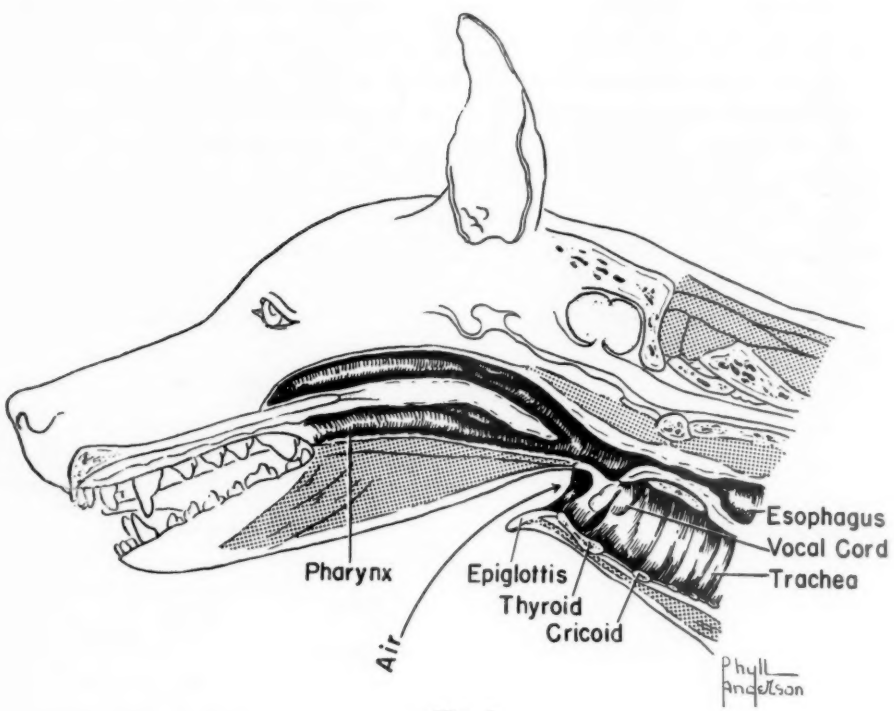


Fig. 2.

Fig. 1.—Midsagittal section of normal dog.
Fig. 2.—Midsagittal section of dog with an exteriorized larynx.

The larynx is under direct vision and it is not necessary to anesthetize the animal for each periodic examination. It is possible to photograph the mucosal surface at very close range (see Fig. 4). With additional photographic equipment, better detail can be obtained. The mucosa of the larynx is now a surface structure and readily accessible. The direct application of drugs or irritants

Fig. 3.

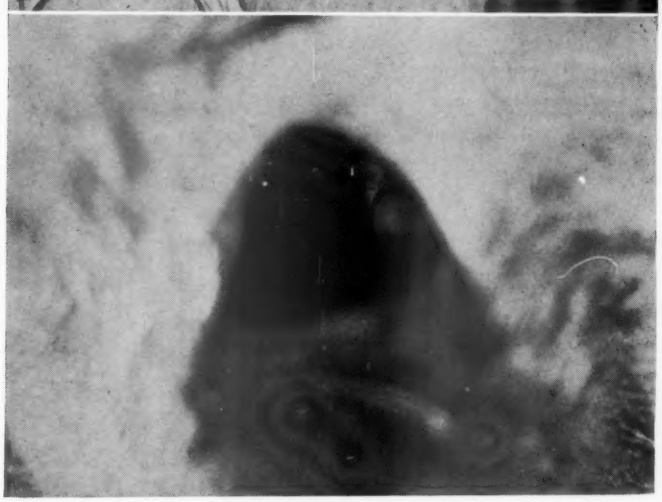


Fig. 4.

Fig. 3.—Rigid frame used to keep neck in extension during immediate postoperative phase.
Fig. 4.—Photograph of posterior half of vocal cords. (Leica, 35 mm. camera; 135 mm. lens with 30 mm. extension tube.)

is possible. If edema or any other organic change should impinge on the airway of the larynx, an adequate airway can be created by tracheostomy at a lower level. This was not required in any of the dogs used to perfect the procedure.

SUMMARY

A simple method of producing a laryngeal preparation in the dog is described. These preparations can be used to study both the direct action of drugs on laryngeal mucosa, and changes in the larynx following systemic therapy.

RELAXED ANTERIOR CRUCIATE LIGAMENT

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A RELAXED cruciate ligament is frequently the cause of continuing disability following routine arthrotomy for internal derangement of the knee. On the basis of this observation, an investigation was undertaken to determine whether cruciate ligament relaxation had been detected preoperatively, during the operation, or postoperatively. During the period from 1940 to 1947, there were from various sources, 350 patients with knee disabilities, and with persistence of symptoms following operation who were examined at the United States Marine Hospital, Staten Island, N. Y. The cause of continuing disability in 120 of these cases was due solely to a relaxed anterior cruciate ligament, associated in sixteen cases with involvement of the internal collateral ligaments.

In a review of 2,300 knee cases with examination during the same period but no operation, it was noted that the disability present in 9 per cent was apparently due to a derangement of the anterior cruciate ligament alone. In an additional 10 per cent of this same large group, relaxation of the anterior cruciate ligament was associated with injury to the internal meniscus or the collateral ligament. When 510 patients who were originally included in the group of 2,300 were subsequently operated upon, 5 per cent were found during the operation to have relaxed anterior cruciate ligament as the cause of disability. An additional 2 per cent which had not been detected preoperatively or during operation were discovered postoperatively.

ETIOLOGY

Accidents in which hyperextension or severe rotation of the knee occur, or in which the femur is driven backward while the knee joint is flexed, are usually responsible for a relaxed anterior cruciate ligament. Derangements of the internal meniscus and the collateral ligaments are also produced in this manner and are therefore often found concomitantly with relaxation of the anterior cruciate ligament. In addition to being stretched, the cruciate ligament may be ruptured partially or completely, or it may be torn from its bony attachments as a result of great violence in which partial dislocation of the knee has occurred. The majority of cases of cruciate ligament injury result from participation in sports, such as baseball, basketball, or football. In industry, cruciate ligament injuries commonly occur in the course of jumping several feet onto the ground or slipping from ladders or scaffolds at low heights. In many of the patients observed, a history of previous knee injury was obtained.

PHYSIOLOGY

The anterior cruciate ligament has its origin in the lateral condyle of the femur and extends into the anterior intercondyloid eminence of the tibia. The ligament is tense during all phases of extension or flexion of the knee joint. The

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lateral stability of the knee is dependent in part upon the proper tension of the anterior cruciate ligament. The relaxation is greatest when the knee joint is in the position of rotation. When the knee is in full extension, there is little or no loss of stability, provided that one of the cruciates or one of the collaterals is intact.

SYMPTOMATOLOGY

Occasionally, rupture of one cruciate ligament may cause no interruption in the function of the knee because of the compensatory action of the collateral ligaments and the increased tonicity of the musculature about the knee joint. In the typical uncomplicated case, no true locking of the knee joint occurs. Occasionally, a complaint of clicking or pseudolocking is elicited. The patient complains of weakness and instability of the knee joint involved. This feeling is often increased by reflex relaxation of the quadriceps muscle which may occur after trauma to the knee. Pain and swelling are commonly noted in addition to these symptoms.

In those cases in which injury of the cruciate ligament and of the internal semilunar cartilage coexist, excision of the cartilage will not correct those symptoms due to cruciate ligament pathology. Those symptoms will persist until the defect of the anterior cruciate ligament is remedied.

DIAGNOSIS

In the typical case of relaxed anterior cruciate ligament, a history of an accident involving the knee is usually elicited. The patient complains of pain and the knee joint is swollen. There is tenderness over the tibial fat pad in the popliteal space. An uncomfortable sensation of instability of the knee joint is present.

Lack of anteroposterior stability, with gliding of the tibia on the femur, is pathognomonic of anterior cruciate ligament injury. The "drawer" sign for integrity of the ligament is carried out by having the patient sit on an examining table with his feet dangling loosely over the side. The examiner sits on a low stool, facing the patient, with his knees at the level of the patient's ankle. In this position, the examiner can easily hold the ankle steadily between his knees while quickly pulling the upper part of the tibia anteriorly. If relaxation or other injury of the anterior cruciate ligament exists, a positive "drawer" sign is elicited when a greater amount of gliding is noted in the injured knee as compared with the sound one. The examiner should always compare the extent of movement of one knee with that of the other knee. An alternate method of performing the "drawer" test is by having the patient lie in the supine position with the thigh flexed 45 degrees and the leg flexed 90 degrees. In this position, the foot is easily fixated on the table while the tibia is jolted anteriorly as described. Occasionally, 5 to 10 c.c. of 1 per cent procaine hydrochloride may be instilled into the joint or general anesthesia may be administered as an aid in eliciting the "drawer" sign. As has been pointed out previously, the unaffected knee should always be used for comparison.

Diagnosis of relaxed anterior cruciate ligament may be made in some instances only at the time of operation. In all knee arthrotomies, the anterior cruciate ligament should be grasped with a shoebuckle hook and the degree of tension of the ligament should be determined with the knee in full extension, mid-flexion, and full flexion. Relaxation of the ligament is readily demonstrated in this manner.

THERAPY

Acute trauma of the cruciate ligament should be treated by complete aspiration of the knee and application of a cast with a minimum of padding. Immobilization of the knee should be carried out in a position of 20 degrees flexion and should be maintained for a period of three months. During this time, the patient may use crutches.

Surgical repair of relaxed cruciate ligament may not be warranted in persons whose occupations are not strenuous and who have little disability. Conservative treatment consisting of exercises which will strengthen the quadriceps musculature, patellar shrugging, and sine therapy may permit such individuals to compensate fairly well and get around satisfactorily. As the quadriceps tendon is considered the keystone of the knee joint, the regime described here is effective in cases of mild relaxed cruciate ligament.

Conservative therapy is usually of no avail in cases of pronounced cruciate ligament relaxation. Unless surgical correction is instituted, the patient may have to become resigned to permanent use of a knee brace. Surgical intervention consisting of the addition of a fascial strand across the same line as that of the anterior cruciate seldom provides better results than conservative therapy. Consequently, a procedure has been devised whereby the anterior spine of the tibia is depressed within the tibial plateau for a sufficient distance to produce a normal tension of the ligament. This corrective measure has produced excellent results in contrast to the previously described procedure.

A medial parapatellar incision is made over the knee. The capsule and synovium are split in the same direction. The entire length of the knee joint is exposed, and at the upper pole, care is taken to undercut the sheath of the vastus internus and not the muscle. The patella is retracted medially and everted upon itself, providing complete exposure of the anterior knee joint. The knee is flexed 90 degrees. If the cartilage is damaged, it is removed. The relaxed anterior cruciate ligament is retracted anteriorly by means of a buckle hook. An osteotome is used to punch out a rectangle of anterior spine bone which is the attachment of the cruciate ligament (see Fig. 1). In instances where the anterior cruciate ligament has been badly frayed, a close examination should be made prior to the preparation of the block of bone so that the entire attachment of the cruciate is present. The block of bone with the intact anterior cruciate ligament is depressed for approximately ½ inch or for a sufficient distance to place the anterior cruciate ligament under tension. If the block has been depressed more than was required, it will return to a site of normal tension after flexion and extension of the knee have been carried out. Should the block be insufficiently depressed, relaxation of the anterior cruciate will persist.

The depressed block is held in position by means of a medium-gauge Kirschner wire which is inserted transversely superior to the attachment of the tendon in the block. We have found screw fixation satisfactory and, frequently, no fixation aside from depression and impaction of the anterior spine is necessary. A cast is applied from the groin to the toes, with the knee in mild flexion. Im-

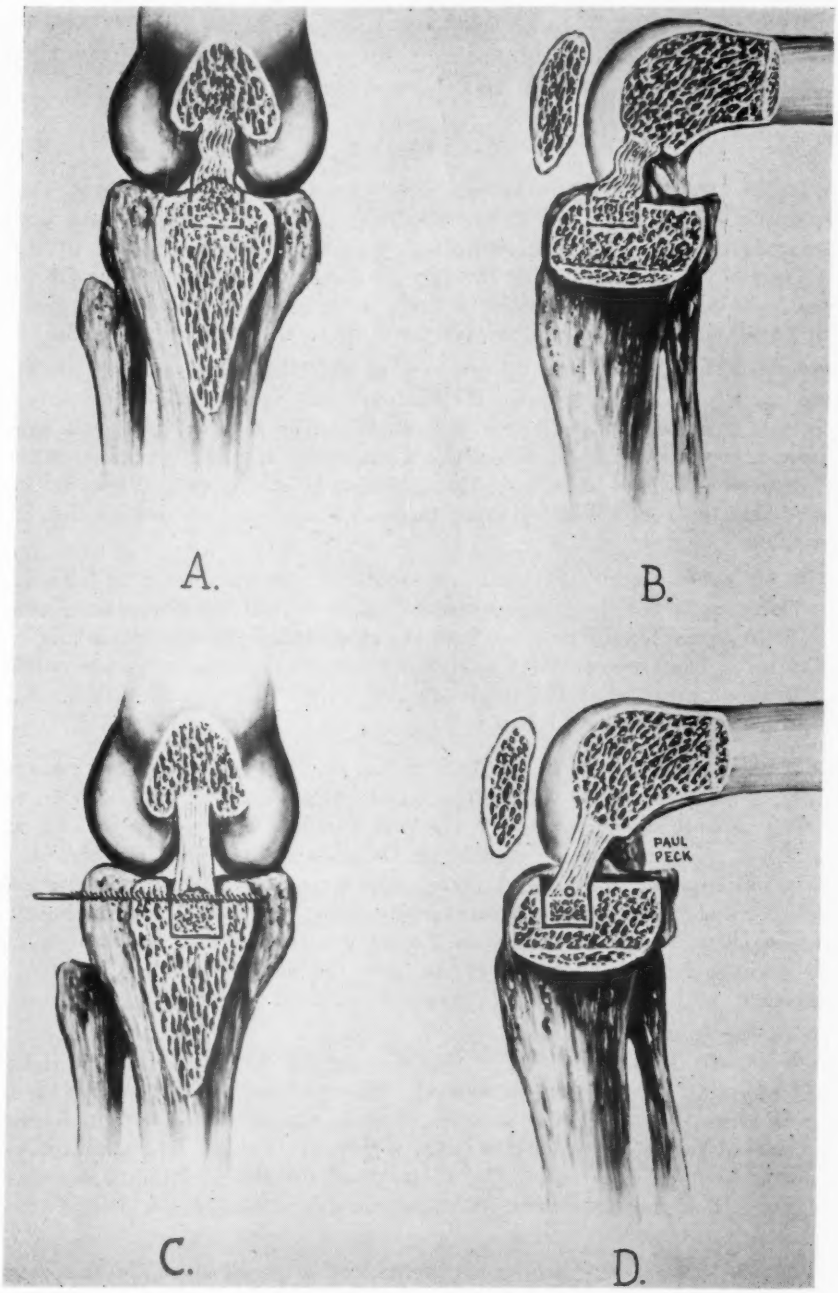

Fig. 1.—*A* and *B*, Showing relaxed cruciate ligament and size of osteotomy. *C*, Showing frontal view with metal fixation of the depressed block. *D*, Lateral cutout view showing the depressed bone fragment and the cruciate ligament under tension.

mobilization is maintained for three weeks. At the end of this period, the cast is split and quadriceps and straight leg-raising exercises are instituted. At the end of five weeks, whirlpool with active and passive exercises is begun. At this time, the patient is supplied with a three-fourths dial knee-control brace, calipered into the heel. With weight-bearing activity, the peg of the brace is shifted from one notch to another. A final free-hinge joint is permitted approximately three months after surgery. The brace is discarded at the end of the third month and is replaced with a light Jones' knee cage. During the entire period, active and passive exercises and sine therapy are carried out.

CASE REPORT

CASE 1 (No. 168479).—J. C., a seaman, aged 42 years, weight 170 pounds, was admitted to the hospital on July 1, 1946. In May, 1945, he was on a ship when a mine exploded and he was thrown in the air. He sustained an injury of the left knee but had little disability. After a two-month period, however, he experienced a sharp pain upon movement. A locking of the knee developed which felt as if the knee were going out of joint. He was given a course of physical therapy without improvement up to the time of admission.

Treatment.—The patient was operated upon July 19, 1946. A medial parapatellar incision was made over the left knee. The capsule was split in the same direction. The anterior cruciate was found to be frayed and relaxed. The anterior spine was removed with its attachment over the anterior cruciate. It was depressed into the cancellous portion of the tip for a distance of ⅛ inch and fixed into position by means of a Kirschner wire. The stability was considered improved following this procedure. A cast was applied to the knee in full extension.

Results.—Four months after surgery, the patient was working on a banana boat and had no complaint regarding the knee. An examination showed the extension of the knee was complete with 10 degree loss of flexion. Stability in an anteroposterior plane and in a lateral plane was normal. There was no joint reaction. Power of the quadriceps was normal. There was no evidence of atrophy of the thighs or the calves. X-ray examination showed bony union of the depressed block of bone.

CASE 2 (No. 163389).—D. D., aged 39 years, weight 180 pounds, fell from a tank on June 9, 1943, landing with his full weight on the right knee and twisting it. The knee began to swell and became very tender. The pain persisted for two weeks. At the time of admission, May 3, 1946, the patient stated that the knee was unstable and gave way, particularly when he was climbing, stepping off curbs, or on steps. Considerable clicking and popping at the knee joint was experienced. On one occasion, about one year before, the knee had locked and he was unable to straighten it. When the leg was rotated with the knee in full flexion, a definitely audible palpable click was elicited over the posterior medial aspect of the knee. He was assigned to limited duties and received sporadic courses of physical therapy and exercises and used a White knee cage.

Treatment.—On May 14, 1946, a parapatellar incision was made over the right knee and the capsule was split in the same direction. The meniscus was markedly macerated and torn. It was excised in toto. The anterior cruciate was thickened with the presence of a sufficiently marked relaxation to elicit a positive "drawer" sign. The anterior spine of the tibia was detached for a distance of 1 by ½ inch and the anterior tibial spine was impacted into the upper end of the right tibia. The patient was discharged on June 6, 1946, with a dial brace.

Result.—The patient returned to his regular work at the end of a four-month period. The knee was stable in an anteroposterior plane. There was no joint reaction of the knee. Motions of flexion and extension were complete. X-ray examination showed the presence of a solid fusion of the depressed graft.

SUMMARY

The incidence, etiology, physiology, symptomatology, diagnosis, and therapy of relaxed anterior cruciate ligament are discussed. As conservative therapy has failed to produce a stable knee in protracted cases of relaxed anterior cruciate ligament, a method has been devised whereby the anterior tibial spine with the attached cruciate ligament is depressed within the medullary substance of the tibia. This corrective measure has produced excellent results in contrast to other available methods. Two case histories are reported to illustrate the efficacy of this procedure. In both instances, the defect was remedied with the result that the patients were able to return to their original work and conduct their regular activities.

RECONSTRUCTION OF INDEX FINGER WITH NAIL TRANSPLANTATION

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IT HAS been repeatedly reported that the incidence of hand injuries is the highest in industrial and domestic accidents. With the rapidly increasing mechanization of our day, hand injuries may be expected to reach a phenomonally high proportion. The hand is obviously the most exposed and most commonly injured part of the human body.

The degrees of physical incapacity consequent to mutilating injuries of the hand, particularly as related to loss of fingers in part or in whole, are variously estimated. Thus, loss of a thumb is considered tantamount to that of half a hand; loss of an index finger of the right hand is considered equal to 15 per cent incapacity, and of the left 10 per cent. The associated psychologic impact, though hardly measurable, is no less disabling.

The surgeon, in constructing a part of a hand, is called upon to carry out techniques to restore function, to minimize deformity, to remove disfiguring scars, and to return the injured person psychologically and physically conditioned for his occupation.

In the planned treatment of a hand injury it is of paramount importance to give thought to the patient's occupation and to the functional diagnosis. A result which may be adequate for a clerk, for example, may not be so for an artisan, a model, or a manicurist. The manual worker, in the main, needs above all a completely functioning hand, the fine cosmetic appearance of which is not of transcendent importance. In the case of a model or an actress, the final cosmetic result is of greater importance than the functional one. Also to be borne in mind are the patient's athletic interests and hobbies.

The objective in reconstruction should be to restore the basic finger-thumb association; that is, the digits should be brought into opposition. The restoration of this function (thumb opposition to the tip of the index finger, middle finger, or ring finger) cannot be too strongly stressed. Even though a minimum of action of the fingers and thumb is obtainable, the patient may have immediately a useful hand for gross purposes, such as the ability to pick up or hold an object.

Various methods are utilizable to restore a digit, namely, transposition of one of the remaining digits of the same hand; procurement of a whole or part finger graft from the other hand,[1] and transplantation of toes for fingers;[2-5] or reconstruction of a finger by tubular pedicle graft, with inserted cartilage or bone graft.[6, 7]

The surgical construction of a lost finger or fingers presupposes on the part of the surgeon a minute knowledge of the anatomy, dynamics, and myomechanics of the hand. The close association of tendons, tendon sheets and fascial planes, nerves and blood vessels, often involves them singly or collectively.

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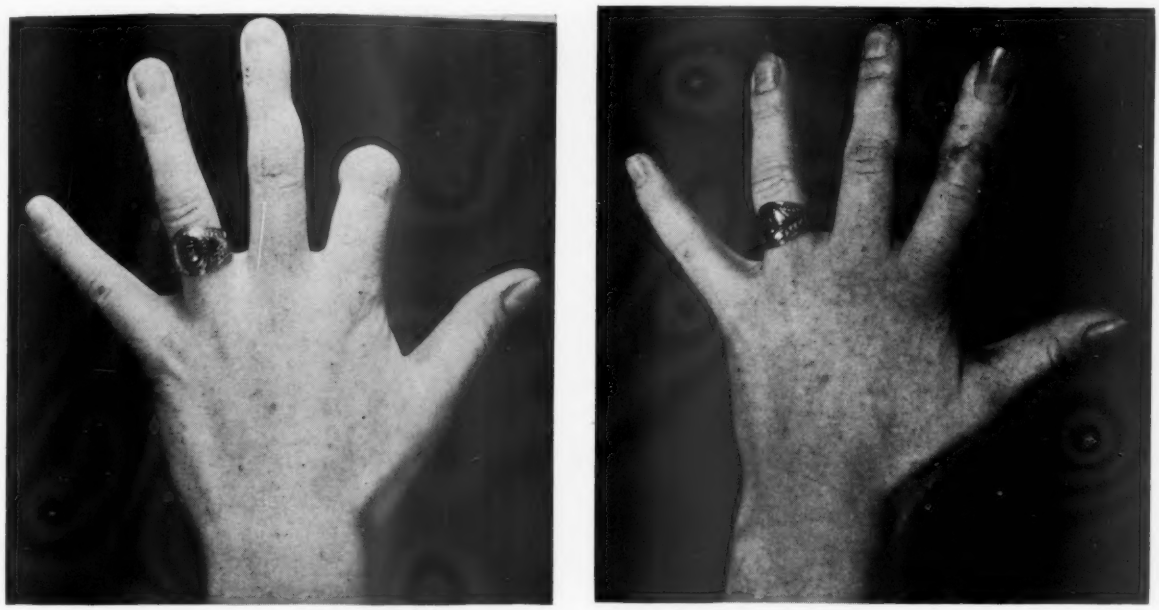
It is always advisable to take roentgenograms of the hand before planning a reconstructive operation.

I have modified the following technique of finger reconstruction with the use of a tubular pedicle graft and insertion of preserved cartilage, followed by transplantation of the toenail (Fig. 1, *A*, and *B*).



A. *B.*

Fig. 1.—*A*, Complete loss through trauma of distal and middle phalanx of left index finger. A short, wide stump of skin and adipose tissue projected about ½ cm. from the end of the proximal phalanx. The remaining part of the proximal phalanx of stump of index finger was functionally normal. B, Reconstructed finger, in extension, with transplanted nail, six months after operation.

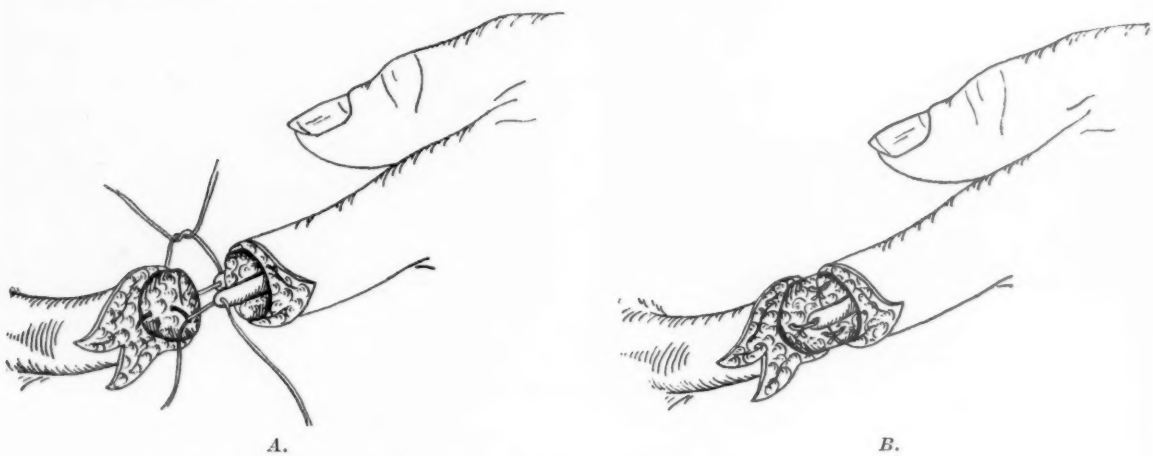
Fig. 2.

Fig. 3.

Fig. 2.—Cartilage implant under skin.
Fig. 3.—Raised tubed pedicle with inserted cartilage.

First Stage.—A pocket for the cartilage implant was made transversely under the skin in the right inframammary fold. A piece of preserved cartilage 1 cm. in diameter and 3 cm. in length, fashioned approximately to the size and shape of a terminal phalanx, was procured and placed in the prepared pocket. Several catgut sutures were drawn through the skin and cartilage at both ends to anchor the implant. The skin incision was closed with several interrupted silk sutures (Fig. 2).

Second Stage.—One month later paralleling incisions of equal length were made in the skin along Langer's lines 1 cm. above and below the cartilage implant. The skin and subcutaneous tissue with the cartilage attached were raised along their length from the underlying fascia. The flap was tubed by suturing the opposing skin edges. The raw area beneath the pedicle was closed by undermining the margins of the skin, and approximating them with interrupted sutures (Fig. 3).



A. *B.*

Fig. 4.—*A*, End of pedicle detached with V incision. Finger stump opened with similar incision; flexor and extensor tendons exposed and chromic sutures passed through the tendons and into cartilage. *B*, Union of pedicle and finger stump by tying sutures.

Third Stage.—Two weeks later the proximal end of the pedicle was detached with a V incision. The donor area on the thorax left by detaching the pedicle was closed by undermining and approximating the skin margins. The finger stump was opened with a V incision on the palmar side. Fibrous tissue was removed from the distal end of the phalanx, leaving sufficient tissue padding. The flexor and extensor tendons of the stump were exposed and dissected free for about 2 cm. Chromic catgut sutures were passed through these tendons and anchored to the cartilage within the pedicles; the two parts were thus approximated, leaving a certain amount of subcutaneous tissue intervening to obviate union of bone to cartilage and also to permit subsequent function (Fig. 4, *A* and *B*).

The skin flaps were closed in position with interrupted sutures of black silk, thereby forming a series of V's around the finger (Fig. 5). The multiple V incisions at the finger pedicle junction assured better surface attachment, blood circulation, and elasticity of the skin at the new phalangeal junction.

Fig. 5.—Finger stump sutured to pedicle, forming series of V's around finger.

Fig. 6.—Section of toenail removed, showing remaining parts of nail intact and vertical slits in cuticle.

Fig. 7.—Suture holding nail in place.

The arm in its entirety was immobilized with a padded wooden splint for ten days, leaving a small open window at the surgical site for periodic checking.

Fourth Stage.—At the end of the ten-day period the remaining pedicle was detached from the thoracic wall by a V incision which passed into the subcutaneous tissue. To fashion the new finger tip, provision was made for adequate length and width of the pedicle flap and for padding. The margins of the donor area on the thorax were undermined and closed by approximation. On completion of the pedicle flap the tissues of the detached pedicle were trimmed and closed to form a well-padded, tapered finger end with Langer's lines placed horizontally across the finger, closely approximating those of the finger stump.

Fig. 8.—Reconstructed finger showing restoration of flexion and ability to hold objects.

Fifth Stage.—The last stage was transplantation of toenail to the reconstructed finger. Two months later a semicircular incision was made at the distal end of the reconstructed finger, and at a site similar to the cuticle of the corresponding finger, to form a pocket for nail implantation. Here the skin was elevated 0.5 cm. The epithelium over the nail area was completely shaved up to the semicircular incision, leaving exposed derma and forming a bed for the transplant.

In removing the nail from the large toe two small vertical slits were made in the cuticle. By blunt dissection the cuticle flap was drawn upward exposing the matrix of the nail. The contour and size of the implant were delimited on

the donor nail and matrix, as well as on the lunular plate. The outlined nail was stripped bluntly from its bed, leaving intact part of the proximal end and the lateral aspects of the donor nail to permit regrowth of the new nail, thus eliminating the subsequent possibility of an ingrown toenail (Fig. 6). The nail, correctly trimmed, was transplanted on the open dermal area with the lunular end and margins of the nail inserted deeply in the semicircular pocket. A silk suture was inserted through one side of the skin overlapping the nail, then over the nail through the opposite flap. In tying the ends the nail was held firmly in place (Fig. 7). The palmar surface of the finger was supported by a padded splint, thus providing additional immobilization and anchorage of the implant. The dressing was left undisturbed for two weeks, after which a similar one was placed for further protection.

CONCLUSION

Flexion of a 90 degree angle and complete extension were obtained because the flexor and extensor tendons were attached to the pedicle graft (Fig. 8).

There was no loss of sensation in the skin of the finger stump. The V incisions used in fashioning the finger pedicle junction provided good surface attachment, good blood supply, and elasticity of the skin.

Cosmetic results were extremely gratifying because the transplanted fingernail remained viable. Langer's lines on the pedicle closely paralleled those of the finger stump. There was consequently inappreciable cosmetic textural change.

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DIPHTHERIA OF THE GRANULATING WOUND; ITS TREATMENT WITH METHYLENE BLUE

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WOUND diphtheria as early (primary) infection can be a very serious occurrence. Years ago it sometimes was seen after tracheotomy performed for diphtheric stenosis of the larynx. Rapid phlegmonous invasion of the adjacent tissues with formation of large fibrinous layers, often accompanied by toxic sequelae, were the most striking features of this kind of wound diphtheria. Quite different is the "secondary" diphtheric infection of the granulating wound. The symptoms generally consist merely in a slight alteration of the granulations. They are covered by a thin layer of whitish or yellowish membranes. The granulations are pale, edematous, and their surface is homogeneous. There exists generally an increased secretion of serous fluid; marginal epithelization does not progress; the newly formed strata lose their contact with the underlying granulations and drift away. Any repercussion on the general state, as fever or toxic symptoms, is nearly always missing. When these wound alterations are present, the suspicion of diphtheria must always arise. But the final diagnosis depends entirely on the bacteriologic examination, which is indispensable. It must be considered further that sometimes the quantity of bacteria is very small; a single examination is, therefore, not always sufficient.

As indicated in this description, the clinical features of wound diphtheria are not distinctive. But as long as the diphtheria organisms do persist upon the granulations, the healing of the wound obviously is impossible. Neither would epidermic transplantation succeed because the grafts could not adhere to the base. Moreover, such a wound is always to be regarded as a possible source of another localized infection, for example, in the throat, for the same individual or for others. The isolation of the patient, when hospitalized, is therefore not less necessary than it is for ordinary diphtheria cases.

The treatment of wound diphtheria is of considerable practical importance. The more so, as wound diphtheria assumes sometimes—as I have seen in Germany and in Turkey generally coincident with an increase of common diphtheria —a real epidemic character.

But this therapeutic problem is more difficult than might be expected. In the first place, the attempt to get rid of this infection by the aid of the specific serum has entirely failed. Considering that this serum is antitoxic and not antibactericidal, the failure of diphtheria antitoxin is not surprising. But also the use of different antiseptic agents which has been recommended for the same purpose, for example, eucupine, iodine (in alcoholic solution), or mercury, or the thermocoagulation of the infected area has not been successful. Therefore, in 1936 Löhr[1] confirmed the opinion, formerly put forward by Weinert,[2] that therapeutic measures against wound diphtheria do not exist practically. Simons[3] and Drugg[4] have pronounced similar opinions. But in reality such a negativistic attitude is not at all justified. For more than twenty-eight years I have been us-

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ing an agent in the management of wound diphtheria which has given such splendid results that the search for other methods has seemed unnecessary. This medicament is pulverized methylene blue.

The idea to use this product in the management of wound diphtheria resulted from experiments I made together with Rosenthal[5] on the absorptive power of granulating wounds. In general, the granulations were able to protect the deeper tissues against many substances which are brought into contact with the wound surface. But a remarkably different reaction is shown against methylene blue. This substance, especially when supplied in finely pulverized form, can penetrate the whole layer of granulations in a very short time without causing the least alteration of their vitality. The coloring matter gets, by this way, to the blood stream and when given in a dose of 0.1 to 0.2 Gm. twenty-four hours later the urine often shows the characteristic blue coloration. In fact, the bactericidal power of methylene blue on the *Corynebacterium diphtheriae* is only a restricted one, as Franz[6] has shown when using in vitro a 1 per cent solution. But when the substance is applied in finely pulverized form the possible concentration is of course much higher and the quick penetration brings the effective agent nearly immediately in contact also with those germs which are localized in the deepest layers.

The practical results I obtained with this method were excellent.[7] In one of the cases communicated in my publication of 1935, the treatment administered previously in another hospital had lasted nearly one whole year without the least result; when methylene blue was given the specific infection ceased in the course of two weeks. My own results have been confirmed by Dieterich,[8] but afterward this method was practically forgotten. To a certain degree technical reasons are perhaps responsible for this failure of my proposal. I have heard occasionally that methylene blue had been used as a solution, whereas satisfactory results can be obtained *only* by applying the pulverized substance.

The time necessary for successful treatment is usually about two weeks. During this period the dressing must be changed every second day. Practically all my patients made a complete recovery. The aspect of the wound changes immediately when the specific infection has ceased. The fibrinous layers disappear; the granulations show a vivid red coloration; the secretion becomes normal and the epithelization begins anew.

Only when the patient's general condition was extremely bad, that is, principally in lethal cases, the local treatment also remained unsuccessful. From the theoretical point of view this fact is interesting, for according to Pulewka[9] (professor of Pharmacology of the Ankara University) the clinical effect of methylene blue cannot be regarded as identical with the reaction shown in vitro, but is probably connected with a biologic activation of the infected tissues.

Since my first communication made upon this matter I have always used this treatment with the same good results. However, this simple method is nowhere mentioned. Recently Georg Wolfsohn[10] (Jerusalem) used it in a case of diphtheric wound infection after prostatectomy; he was under the impression that this treatment led to great improvement. Therefore, it seemed to me worth while to direct attention once again to this kind of treatment.

TABLE I

NUMBER	SEX	AGE (YR.)	PROTOCOL NUMBER	NAME	PRIMARY CONDITION	LENGTH OF TREATMENT (DAYS)	RESULT
1	F	50	15136/47	Fat.	Operation for cancer of breast	18	Cured
2	F	7	1469/48	Ces.	Multiple burns	10	Cured
3	M	9	6206/48	Has.	Ulcer following noma of face	14	Cured
4	M	7	7148/48	Ibr.	Chronic osteomyelitis of femur	28	Cured
5	M	23	7686/48	Cem.	Femur exarticulation for hip tuberculosis	19	Cured
6	M	13	14387/48	Sul.	Ulcer following noma of face	14	Cured
7	F	35	14620/48	Em.	Amputation for tuberculosis of foot	10	Cured
8	F	20	14691/48	Ay.	Amputation for knee tuberculosis	10	Cured
9	M	15	16192/48	Niy.	Chronic osteomyelitis of femur	21	Cured
10	M	7	17261/48	Bek.	Ulcers resulting from burns of leg	14	Cured

To show the effect of this method in a more detailed way I have reunited in Table I the ten last cases in which this treatment has been used.

Table I suggests that the results were uniformly satisfactory. Also clinically the disappearance of the specific germs was regularly followed by a rapid amelioration of the wound. The average time of treatment was 15.8 days.

In the cases listed this time varied between 10 and 28 days. In reality the average time needed for the elimination of the specific infection was certainly less than is suggested by the figures given. In many instances the time which elapsed between a negative and a prior-positive test was often of one week's duration or more. In other words, a more frequent bacteriologic study of the wound probably would have reduced the disappearance interval of the diphtheria organisms from the wound.

SUMMARY

Diphtheria of the granulating wound can be successfully treated by pulverized methylene blue. Based upon experimental researches made, together with Rosenthal, the author has employed this method for twenty-eight years. The results have been excellent. Inasmuch as this mode of treatment has remained practically unknown, the reporting of an enlarged experience with its use appears justified.

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Case Reports

PERSISTENT CERVICAL THYMUS GLAND; THYMECTOMY

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PERSISTENCE of thymic tissue in the neck is known to occur along the course followed by the gland in its descent in the embryo. In order to understand this abnormality, the following brief embryologic review of the thymus gland is presented (Patten[7]).

The thymic primordia appear late in the sixth week as ventral outgrowths of the third pharyngeal pouches. By the early part of the seventh week the primordia have enlarged strikingly, but they still retain their connection with the pharyngeal pouches and remain associated with the pair of parathyroid glands derived from the third pharyngeal pouches. During the seventh week they increase rapidly in bulk, and their distal tips begin to approach each other as they swing toward the midline just caudal to the thyroid primordium. By the middle of the eighth week the distal tips of the thymic primordia have made contact with each other and have started to slide down under the sternum into the mediastinum, where they lie in contact with the parietal pericardium.

In a study of developmental abnormalities of the thymus and parathyroids, Gilmour[2] reported 13 post-mortem studies of cases showing thymic tissue in unusual positions; 11 were infants, of which 5 were stillborn. In one case there was bilateral and in another unilateral hypoplasia of the thymus, with complete absence of descent from the position in early embryonic life high in the neck; in the case of unilateral hypoplasia the other thymus was enlarged and had crossed over into the thorax on the opposite side. Four cases of left-sided partial failure of descent were found, 2 with the thoracic thymus extending high up into the neck, and 2 with an elongated accessory portion of the thymus passing into the neck from a short distance above the upper pole of the main thoracic thymus. Inclusions of thymic tissue within the thyroid were found in 7 cases. In a review of the literature of the subject, Gilmour[2] found 13 post-mortem studies of 5 cases of partial failure of descent of the thymus, 3 cases of accessory thymic tissue in the neck, 2 cases of inclusions of thymic tissue within the thyroid, 2 cases of absence of descent of the thymus (1 unilateral and 1 bilateral), and 1 cystic thymus associated with a parathyroid. There are 2 other reports of thymic cysts in the neck (Hyde, Sellers, and Owen[3] and Speer[8]).

The following case is the first persistent cervical thymus gland due to partial failure of descent in which thymectomy was performed.

REPORT OF A CASE

History.—S. S., a boy aged 9 months, was admitted to the Mount Sinai Hospital on Feb. 10, 1948. The infant was born at term, weighing 7 pounds 7 ounces. Growth and development were normal. From the time the child was 1 month of age the mother had

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noted a bulge in the midline of the lower part of the neck, varying in size with respiration. Occasional choking after feedings occurred during the month prior to admission to the hospital, and these episodes increased in frequency.

Physical Examination.—The infant was well developed and well nourished, weighing 22 pounds 13 ounces. The temperature was 99° F. There was no abnormalities of eyes, ears, nose, throat, heart, lungs, or genitals. There was a hemangioma of the right calf. Examination of the neck revealed a bulge in the suprasternal region which was soft, and which varied in size with respiration. A small firm mass was palpable over the lower cervical trachea.

A roentgenogram of the chest revealed a wide shadow of the superior mediastinum, characteristic of thymus gland enlargement; the trachea was displaced to the right side. There was no change from a roentgenogram of the chest taken three weeks prior to admission (Fig. 1).

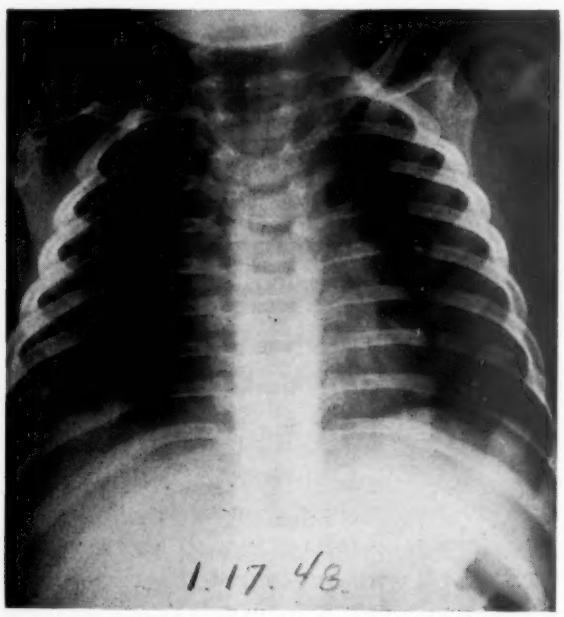

Fig. 1.—Roentgenogram of the chest taken three weeks prior to the patient's admission to the hospital, showing a wide shadow in the superior mediastinum, and a displacement of the trachea to the right side.

Operation was performed by one of us (E. E. A.) on Feb. 11, 1948. With the patient under intratracheal ether anesthesia, a 6 cm. transverse low cervical incision was made. The sternohyoid and sternothyroid muscles were retracted, exposing a firm, yellowish-white, encapsulated mass, about 2.5 cm. in diameter, overlying the trachea. The mass was excised from the surrounding structures, and was found to extend through the superior aperture of the thorax, behind the manubrium of the sternum, into the superior mediastinum. Branches of the inferior thyroid veins were ligated. The mediastinal portion of the mass presented two well-defined lobes, joined at their proximal aspect by the mass in the neck. The lobes were about 8 by 4 cm. in diameter, and of the same color and consistency as the cervical component, except that the lower portion of the left lobe was reddish in color. The mass passed over the left innominate vein and the trachea. The pleurae were not seen. The entire mass was excised from the anterior mediastinum. The superficial fascia and skin of the cervical incision were closed with interrupted sutures of 00000 silk. There was no respiratory difficulty during operation.

*Pathologic Report.**—The specimen (Fig. 2) consisted of a thymus gland weighing 25 Gm. It presented two well-defined lobes which were joined at their proximal extremity,

*Done by Dr. Paul Klemperer and Dr. Sadao Otani.

giving the specimen a roughly triangular shape. The gland was lobulated over its upper portion, and in this area it had a yellowish-white, fatty-like appearance. The lower portions of the lobes had scalloped margins, and were reddish-pink in color, which was most marked over the larger left lobe. The capsule was absent over a portion of the posterior aspect of the gland. The gland was moderately firm in consistency. The cut surface of the gland revealed a coarsely lobulated, smooth, yellowish-white, fatty-like surface, throughout which several areas of hemorrhage were scattered; there were several small focal areas of yellowish pigmentation in the upper portion of the right lobe. On microscopic examination of sections from different parts of the gland a similar histologic picture was seen (Fig. 3). The cortical substance presented closely packed lymphocytes. The medullary substance consisted of lymphocytes, the larger reticular cells, and groups of concentrically arranged epithelioid cells, the thymic corpuscles of Hassall.

Fig. 2.—Photograph of surgically resected thymus gland, showing the cervical and mediastinal components of the gland.

Course.—There was a rise in temperature to 103° F. four hours after operation, dropping to 101.4° F. eight hours later. During the first day the temperature ranged from 100° to 102° F. About twenty-eight hours after operation there was marked dyspnea, subcostal respiratory retraction, noisy rapid respirations, a high-pitched inspiratory wheeze, and pallor. Examination of the chest revealed resonance on percussion; the breath sounds were diminished on the left side, and inspiratory wheezes and coarse inspiratory and expiratory rhonchi were heard on both sides, more marked on the left side. A roentgenogram of the chest

twenty-nine hours after operation (Fig. 4) revealed a left pneumothorax with a 50 per cent collapse of the left lung, and herniation of the left pleural cavity into the mediastinum. The heart and particularly the upper mediastinum were displaced to the right, and a small amount of air was present in the right superior mediastinum. The infant was placed in an oxygen tent; 5 per cent carbon dioxide inhalations were given every two hours and penicillin (10,000 units) every three hours. During the second postoperative day the temperature ranged from

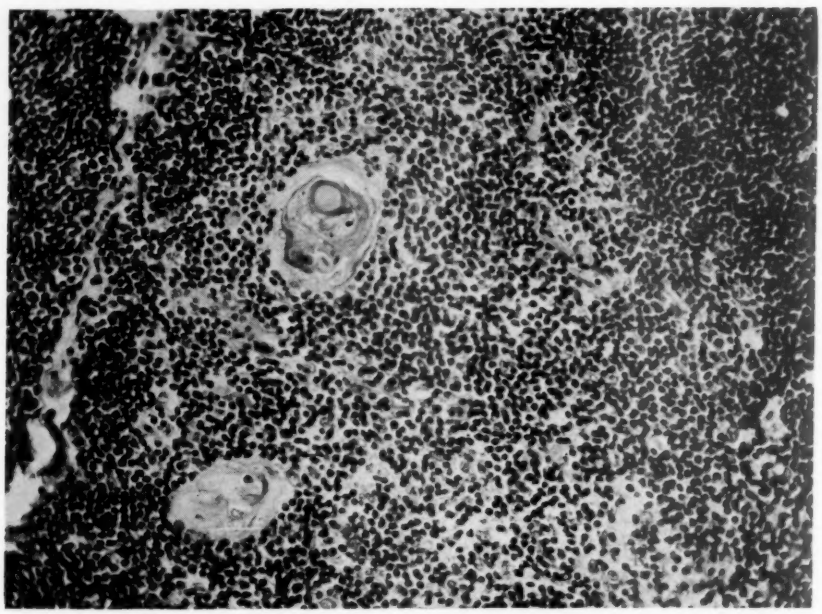

Fig. 3.—Photomicrograph (×200) showing histologic detail in resected thymus gland.

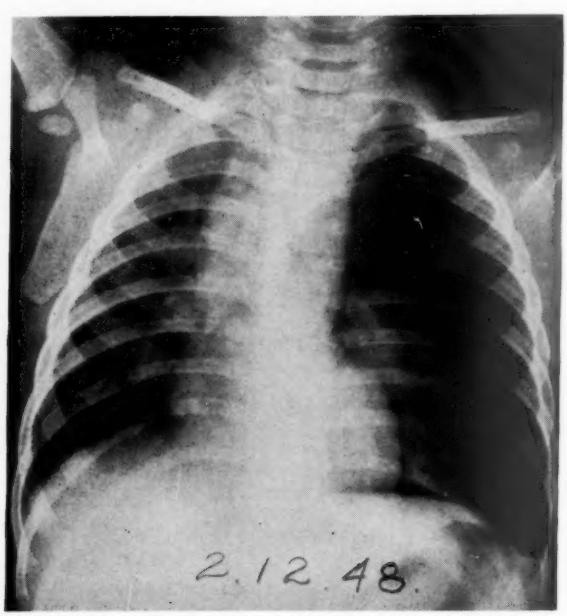

Fig. 4.—Roentgenogram of the chest taken twenty-nine hours after the operation, showing a left pneumothorax with collapse of the left lung, herniation of the left pleural cavity into the mediastinum, and displacement of the heart and upper mediastinum to the right side.

99.2° to 101° F. There was some respiratory difficulty, manifested by inspiratory stridor and subcostal retraction, but the respirations were slower and easier. The infant's condition considerably improved when he sat up out of the oxygen tent; the respirations became slower, the color improved, the stridor subsided, and the infant was playful. Thereafter, he was left sitting up out of oxygen when awake, and replaced in the oxygen tent when asleep. The hemoglobin content was 11.5 Gm.; the leucocyte count was 15,750, with segmented polymorphonuclear leucocytes 50 per cent, nonsegmented polymorphonuclear leucocytes 35 per cent, lymphocytes 40 per cent, myelocytes 3 per cent, and basophils 1 per cent. During the third postoperative day the temperature ranged from 99.2° to 100.6° F. While sitting up, the infant was not dyspneic and the respiratory wheezes and rhonchi were not heard,

Fig. 5.—Roentgenogram of the chest taken seven days after the operation, showing absorption of the left pneumothorax, and a normal superior mediastinum.

but the inspiratory stridor returned while lying down. The oxygen tent and penicillin (270,000 units) were discontinued. On the fifth postoperative day the temperature rose to 102° F., dropping to 100.4° F. in eight hours. The temperature remained normal after the sixth postoperative day. The leucocyte count dropped to 9,800. A roentgenogram of the chest on the seventh postoperative day (Fig. 5) revealed absorption of the left pneumothorax; the superior mediastinum was not widened. The wound healed by primary union. The infant was discharged on the ninth postoperative day.

At follow-up examination when the patient was 20 months old the weight was 28 pounds and the height 34 inches. Roentgen examination of the chest and upper and lower extremities revealed no abnormalities; there was normal development of the epiphyseal and carpal centers of ossification.

COMMENT

"No structure of the body is less understood, nor, with few exceptions, had more functions attributed to it, than the thymus gland" (Nelson[4]). The role of the thymus gland as a causative factor in respiratory obstruction is not clear. Parker,[6] in 1913, reviewed the literature on forty-six thymectomies in children, varying in age from 23 days to 5 years, with dyspnea or suffocative attacks. The mortality was 35 per cent. The weight of the gland varied from 2 to 21.5 Gm., with an average of 8.6 Gm., in the fifteen cases in which the

glands were weighed. On the other hand, Nelson[4] has seen a thymic tumor which filled nearly one-half of the thoracic cavity without causing any evidence of obstruction to respiration. There are many conditions other than an enlarged thymus which are the causative mechanisms of respiratory obstruction in infants. In the case reported, the tracheal compression was due to pressure at the junction of the cervical and thoracic components of the gland at the suprasternal notch. There is a marked variation in weight of the normal thymus, from 4 to 31 Gm. in the age group of the case reported (Boyd[1]).

To date no effects have been reported upon the growth and development of the infant as a result of thymectomy. Follow-up studies of the cases reported by Parker[6] were inadequate. A variety of symptoms and pathologic changes have been reported in thymectomized animals; many of these changes were the result of chance variations, of the effects of confinement or other unfavorable environmental influences, unsuitable food, or disease in animals whose vitality already had been lowered by the shock of a severe operation. Park and McClure[5] performed thymectomies on twenty-four puppies which were carefully observed for periods up to 1¼ years after operation. Their conclusions were as follows: (1) The thymus gland is not essential to life in the dog; (2) extirpation of the thymus produces no detectable alteration in the hair, teeth, contour of the body, muscular development, strength, activity, or intelligence of the experimental animal; (3) extirpation of the thymus probably does not influence growth or development; the possibility that it may cause retardation in development and delayed closure of the epiphyses, however, cannot be excluded absolutely.

SUMMARY

The first case of persistent cervical thymus gland due to partial failure of descent in an infant in which thymectomy was performed is reported.

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ANLAGE TUMORS OF THE SALIVARY GLAND TYPE IN UNUSUAL SITES

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ANLAGE tumors of the salivary gland type are usually located in or near the parotid or the submandibular glands, and occasionally in or near the sublingual glands. They also may occur elsewhere about the face, along or near the lines of fusion of embryonal facial fissures. Anlage tumors of the salivary gland type have also been observed in sites distant from the head. According to our survey about twenty such neoplasms have been reported to date. Of these, twelve were on the upper extremities (ten on fingers and hands,[1-10] two on the forearm[3, 11]), three on the lower extremities (shin,[11] calf,[12] and thigh[13]), and one each in the inguinal region,[14] the vulva,[15] over the sternum,[16] and in the mammary gland.[16] The fact that these neoplasms occur in locations other than the head suggests that their development is not dependent on their proximity to salivary glands. In this paper observations are reported on three anlage tumors of the salivary gland type that occurred near the eyes, and on three which were distant from the head: one over the sternum, one in the mammary gland, and one on the back.

REPORT OF CASES

CASE 1.—W. W., a 49-year-old Negro, was admitted to the University of Oklahoma Hospitals Oct. 23, 1946, because of poorly controlled diabetes mellitus of about one year's duration. A small mass had been present in the center of the left eyebrow since childhood. The mass was nontender, movable, and 2 cm. in diameter. This was excised† Nov. 12, 1946. The wound healed without complication and when the patient was last seen, Sept. 24, 1948, there was no recurrence of the growth.

The specimen removed (S-1648-46) consisted of an elliptic portion of dark skin 3 by 0.8 cm. with a firm, well circumscribed nodule 3 by 2 by 1.5 cm. beneath it. The skin was movable over the nodule. When cut, it gave a sensation of grating. On the cut surfaces within a mottled yellow-white tissue there were numerous cavities from 0.5 to 1.5 cm. in diameter containing a brown, jellylike substance. Microscopic preparations from various parts of the growth disclosed a barely perceptible delicate capsule separating the growth from the deeper layers of the corium. The growth itself was composed of sheets of epithelial cells forming no particular pattern and containing occasional spaces or pseudolumina. They were imbedded in a fairly dense hyalinizing fibrous connective tissue stroma. The epithelial cells had round or oval nuclei within a cytoplasm having indistinct borders. Elsewhere there were large lumina varying in size and shape and lined by flat cells. These contained an amorphous pink-stained material which in some lumina had slitlike spaces bordered by giant cells of the foreign body type and large mononuclear cells containing golden yellow granules. In some of the cell nests the nuclei were arranged in streams. Groups of apparently epithelial cells were also scattered within an amorphous ground substance resembling cartilage (Fig. 1). In some fields the connective tissue was loose and appeared young or embryonal; elsewhere it appeared more mature and hyalinized. An occasional lumen was lined by stratified squamous epithelium with sheets of keratin shed into the lumen.

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CASE 2.—J. W., a 64-year-old white man, was admitted to the University of Oklahoma Hospitals, May 30, 1948. He complained of a small, nontender mass which had been present on the right lower eyelid for forty years, and which, during the past three years, had increased progressively in size. Four months prior to admission a crust had appeared on the surface of the mass. Examination revealed in the right lower eyelid a firm, nontender mass 3 by 2 cm. which was crusted on the surface. The eyelid was slightly everted (Fig. 2). The mass was excised.* When the patient was last seen, July 3, 1948, the wound was well healed.

The specimen removed (S-1032-48) consisted of a globular mass 2 by 2.5 by 2.2 cm. Two-thirds of it was covered by delicate skin. The center of the skin surface over an area 2 by 1.6 cm. was rough and appeared raw and denuded. On the cut surfaces there was a spongy appearance with scattered yellow and gray opaque areas containing minute spaces filled with liquid. Microscopic preparations disclosed nests and strands of epithelial cells with large, vesicular, deeply stained nuclei and a hardly discernible cytoplasm arranged in streams or whorls (Fig. 3). In places there was a tendency for concentric arrangement with sheets of keratin in the center. Elsewhere two rows of cell nuclei lined a space filled

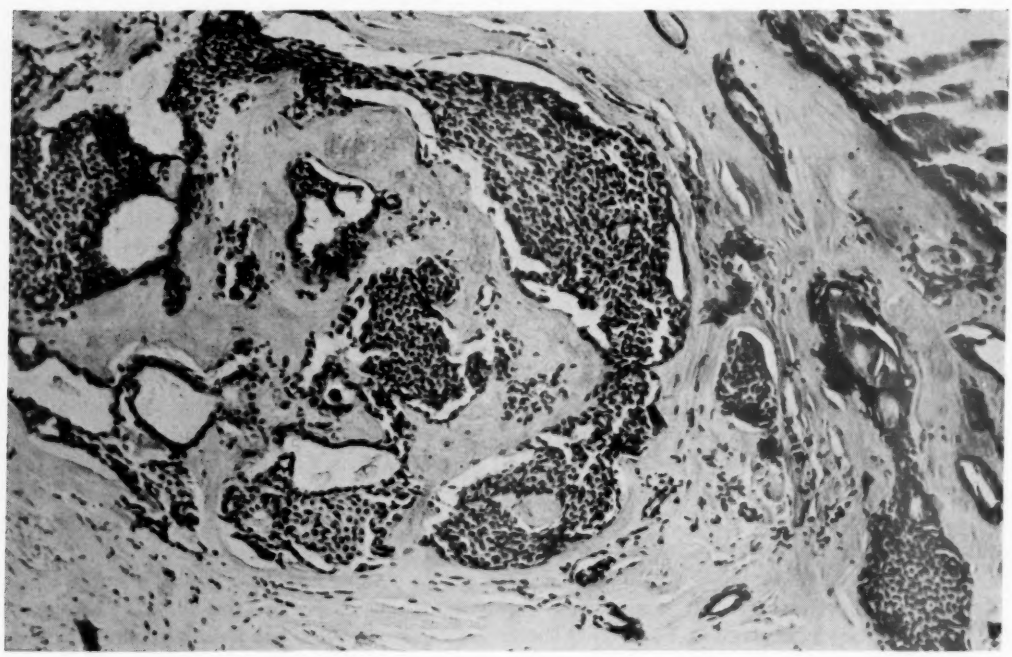

Fig. 1 (Case 1).—Microscopic appearance of an anlage tumor in the left eyebrow of a 49-year-old Negro. (×85.)

with deep pink-stained material. Here and there the cells were within a pink-stained ground substance or a light-stained ground substance resembling cartilage. There were groups of adipose tissue cells. In the pink-stained fields there were some lavender-stained granular deposits.

CASE 3.—G. H., a 52-year-old white man, was seen at the University of Oklahoma Hospitals, Nov. 10, 1948, complaining of a mass in the left lower eyelid. This had been present for about three years. It had increased in size following his attempt to remove it six months previously. Examination revealed a nontender, movable mass 1 by 0.8 by 0.4 cm. in the lateral portion of the left lower eyelid. The mass was biopsied† and the patient has not since been seen.

*By Dr. Hal A. Burnett.
†By Dr. Harrell C. Dodson.

The specimen obtained (S-2093-48) consisted of two fragments of firm, gray-white tissue each about 0.3 cm. in diameter. In microscopic preparations, there were sheets and nests of epithelial cells within a connective tissue stroma. The epithelial cells had round or oval nuclei within a hardly discernible cytoplasm. The stroma was composed in places of a fibrillar

Fig. 2 (Case 2).—Appearance of the growth in situ of an anlage tumor of the lower eyelid in a 64-year-old white man.

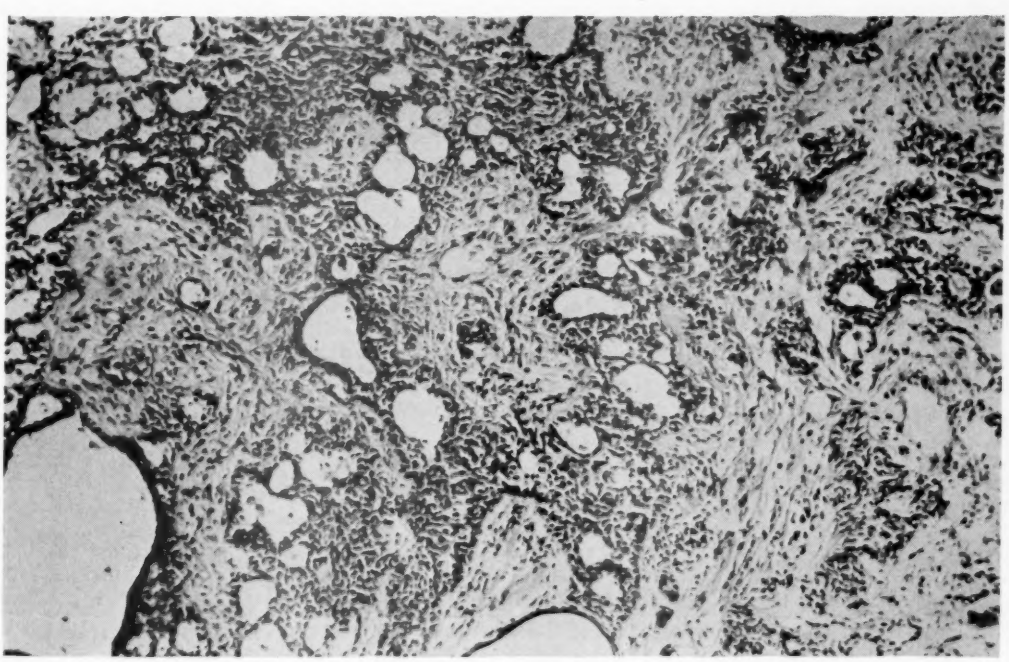

Fig. 3 (Case 2).—Microscopic appearance of the growth shown in Fig. 2. (×85.)

ground substance containing only occasional cell nuclei, the cytoplasm of which faded into the ground substance. Strands of epithelial cells formed a lacelike pattern within this ground substance adjacent to the larger cell masses.

CASE 4.—J. T., a 79-year-old white man, was admitted to the University of Oklahoma Hospitals, April 8, 1948. He stated that for the past forty years a nontender mass had been present in the right mammary gland. The mass had increased slowly in size, had never been painful, and no discharge from the nipple had ever been noted. Examination revealed a firm, nontender, freely movable mass 3.5 by 2.5 cm. in the right mammary gland just beneath the nipple. The axillary lymph nodes were not palpably enlarged. No changes were noted about the left mammary gland. The right mammary gland with the mass was excised,* April 12, 1948. When the patient was last seen, July 22, 1948, the incision was well healed and there was no evidence of recurrence of the growth.

The specimen removed (S-658-48) consisted of the right mammary gland measuring 9 by 4.5 by 2.2 cm. and weighing 35 Gm. One surface was covered by an elliptic portion of skin, 9 by 4.5 cm. In the center of this was the nipple, 1 cm. in diameter, and elevated 0.4 cm. above the surface. The areola was 0.6 cm. wide. There was a globular, slightly lobulated, well-circumscribed firm mass 3 by 2 cm. immediately below the nipple (Fig. 4). On the cut surfaces the mass bulged somewhat, was yellow gray, had a lobular pattern with occasional areas of red-brown discoloration. Beneath the nipple and near the adjacent margin of the growth there was a gray-white area 0.7 cm. in diameter which when cut gave a grating sensation. In microscopic preparations (Fig. 5), sheets and nests of epithelial cells with round or oval nuclei within a scanty cytoplasm were in a loose connective tissue stroma. The periphery of the growth was delimited by a hyalinizing, fibrous connective tissue capsule. Scattered through many fields were lavender-stained concentric bodies. Elsewhere lumina were lined by cuboidal cells. These were within a pink-stained, dense or loose, fibrillar ground substance. Other spaces were lined by several rows of cell nuclei or by columnar cells. Over extensive areas the cellular pattern was blotted out by hyaline change. No areas of cartilage or osseous tissue were seen.

CASE 5.—J. M., an 84-year-old white man, was seen at the University of Oklahoma Hospitals, June 29, 1948. He stated that six years previously a small "cyst" over the lower sternum had been cauterized, but the lesion persisted and periodically drained a thick, white material. Examination revealed a raised, purple, nontender, firm, freely movable mass 1 cm. in diameter over the lower sternum. The mass was excised† June 29, 1948. The wound was healing well when the patient was last seen, July 3, 1948.

The specimen removed (S-1224-48) consisted of an elliptic portion of skin 3.5 by 2 by 1.3 cm. In the center was an irregular, gray-white nodule 1.2 cm. in diameter elevated 0.3 cm. above the surface. On the cut surfaces there was a gray-white, firm mass 1.2 by 0.9 cm. It consisted of lobules up to 0.5 cm. in diameter. Microscopic preparations disclosed sheets of neoplastic cells in a loose or more dense, hyalinizing, fibrous connective tissue stroma. Here and there the epithelial cells formed acinar or tubular structures lined by flat, cuboidal, or columnar cells. Some of the nests were composed of cells with round or oval nuclei in a halolike cytoplasm. These were in streams or whorls in a scanty stroma. Elsewhere strands and nests of epithelial cells formed no particular structures and appeared within a pink-stained ground substance. Again other nests of cells had a pink-stained cytoplasm and eccentrically placed nuclei not unlike the cells in the hypophysis. In still other fields lumina or pseudolumina were filled with a pink-stained vacuolated or scalloped colloid of varying shades (Fig. 6).

CASE 6.—H. E., a 79-year-old white man, was seen at the University of Oklahoma Hospitals, Dec. 3, 1948. He stated that about four years previously a small mass appeared in the right upper lumbar region. This had increased progressively in size, but had caused no discomfort. One year before it had become tender to touch. Examination revealed a

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†By Dr. Phillip Kouri.

Fig. 4 (Case 4).—Cut surface of the right mammary gland exposing the growth in a 79-year-old white man.

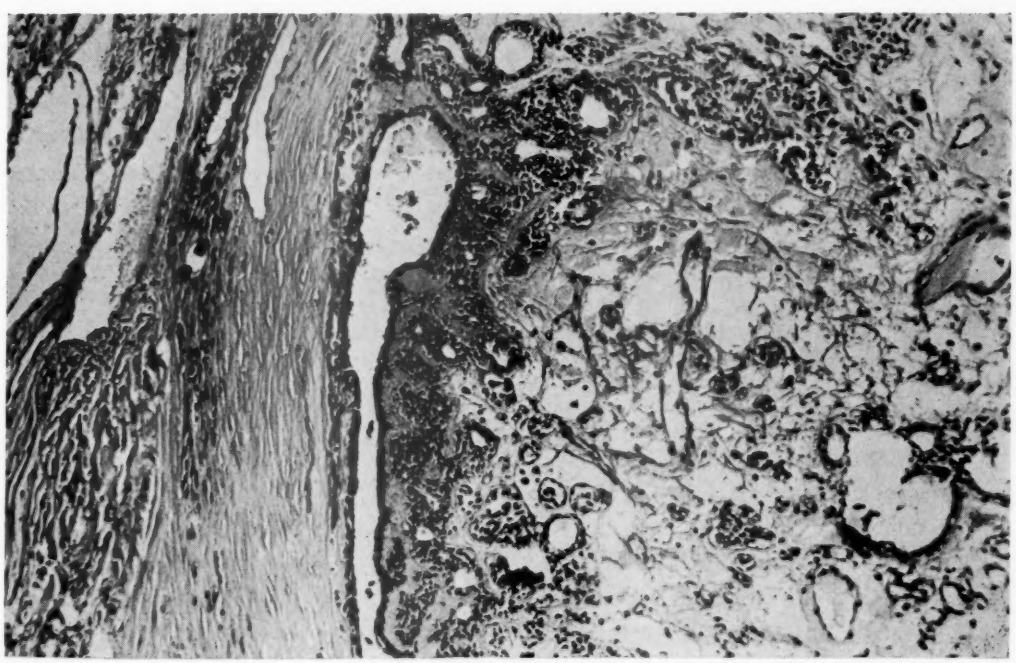

Fig. 5 (Case 4).—Microscopic appearance of the anlage tumor of the mammary gland in Fig 4. (×85.)

tender mass, 10 by 8 by 6 cm., beneath the skin of the right lumbar region. It was firm and freely movable over the underlying structures. The mass was excised* Dec. 9, 1948. The wound was healing well when the patient was last seen, Dec. 16, 1948.

The specimen removed (S-2303-48) consisted of an elliptic portion of tissue, 11 by 7 by 5.5 cm., covered with light skin. At one end of the skin surface there was a rough gray area 0.5 cm. in diameter elevated 0.2 cm. The opposite surface was raw, with lobules of adipose tissue attached. On the cut surfaces there were several cavities up to 3 cm. in diameter containing dark red fluid. Bordering these cavities was soft and firm gray-yellow tissue. In microscopic preparations there were strands and nests of apparently epithelial cells within a scanty, loose, partly hyalinized connective tissue stroma containing blood vessels.

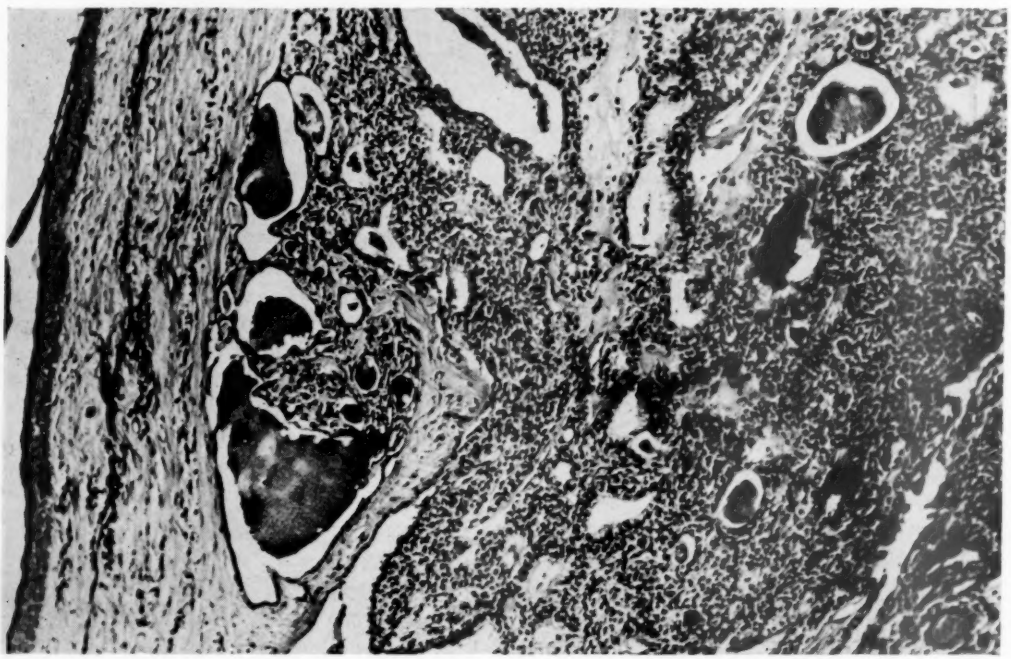

Fig. 6 (Case 5).—Microscopic appearance of the anlage tumor over the sternum of an 84-year-old white man. (×85.)

Epithelial cells enclosed various sized slitlike, round, or oval spaces. Extensive areas of necrosis were discernible. An apparent condensation of fibrous connective tissue formed a capsule at the periphery. In other preparations strands of epithelial cells were seen in a fibrillar ground substance resembling mucin or in a pink-stained ground substance resembling cartilage. The apparently epithelial cells faded into cartilage cells.

COMMENT

The neoplasms herein recorded are essentially similar in their microscopic structure. In most of the growths, neoplastic epithelial (ectodermal) and neoplastic nonepithelial (mesodermal) elements can be clearly distinguished, with the usual intimate mixture of the two. Although they resemble those neoplasms arising in connection with the salivary glands, they are of less complex pattern, and the epithelial elements usually predominate.

The likely derivation of the anlage tumors of the salivary glands is from embryonal rests of the ectoderm, the anlage having separated at a stage when the cells as yet had not acquired their dominant characteristics as ectodermal or

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mesodermal cells.[17] The pattern of imitation of tissue or organ structures which such neoplasms reveal is determined by the cell rests from which they were derived.[18] The growths herein described are similar in structure and behavior to those arising in connection with the salivary glands. This supports the contention that they, too, are of anlage origin.

Anlage tumors arising in other locations as well as those arising in connection with the salivary glands are benign neoplasms, though at times they may become locally invasive. When they occur in sites other than the head, their complete removal is more readily accomplished, thereby minimizing or eliminating the chances of recurrence.

SUMMARY

Anlage tumors of the salivary gland type usually occur in connection with the salivary glands, or about the face along or near the lines of fusion of embryonal facial fissures. They have also been observed in sites distant from the head. Observations on six anlage tumors are recorded: three about the eyes, one over the sternum, one in the mammary gland, and one over the back. The tumors over the sternum and in the mammary gland are the second anlage tumors reported in these sites; that on the back is believed to be the first.

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ISLET-CELL ADENOMA, WITHOUT HYPOGLYCEMIA, CAUSING DUODENAL OBSTRUCTION

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INTRODUCTION

APPROXIMATELY 20 per cent of the islet-cell adenomas or nesidioblastomas cause symptoms of hypoglycemia but rarely any other perceptible signs. Unless the nesidioblastoma produces hypoglycemia, it is usually not discovered until autopsy. Seventy-five per cent of these tumors are located in the body and tail of the pancreas, and usually are not large enough to cause symptoms by pressure. It is most unusual for an islet-cell adenoma to effect duodenal obstruction, since the usual location of the tumor is not in the head of the pancreas where this condition could result and since the size of the tumor is seldom sufficient to cause pressure symptoms. This report concerns a patient who had a large nesidioblastoma in the head of the pancreas which caused symptoms of obstruction in the first part of the duodenum without hypoglycemia.

The first case of islet-cell tumor associated with hyperinsulinism to be diagnosed clinically was recorded by Wilder and associates[1] in 1927. Previously, approximately 20 cases of adenoma or hypertrophy of the islet cells had been reported from autopsy examinations. From 1927 to 1944 an estimated 149 cases of islet-cell adenomas were reviewed.[2, 3, 4]

In almost all the recorded cases of nesidioblastoma, the patients were operated upon because of symptoms of hypoglycemia. However, it is estimated that only about 20 per cent of the cases of islet-cell adenomas do have functioning islet-cell tissue in the adenoma and, consequently, hypoglycemia. The other 80 per cent of the patients with nesidioblastoma are not subjected to surgery, because they produce no symptoms referable to the tumor. Pappenheimer[5] discovered islet-cell adenomas in 5 out of 4,010 consecutive autopsies with indications of hypoglycemia in only 1 case. Campbell, Graham, and Robinson[6] stated that the incidence of nesidioblastoma was 1 in 800 or 1000 autopsies, but that related hypoglycemia occurred in only 20 per cent of these cases of nesidioblastoma. Duff[7] further stated that hypoglycemia associated with an islet-cell adenoma is rare in patients over 60 years old.

Multiple adenomas were observed in 12 to 15 per cent of the cases.[2, 7] These tumors vary in size from 1 mm. to one measuring 15 cm. and weighing 500 Gm. reported by Brunschwig.[8] Duff[7] related that hypoglycemia symptoms have not been observed in association with islet-cell adenomas of a diameter of less than 1 cm. Despite the fact that cells may invade blood vessels locally

The surgery was done by William E. Neville, M.D. The pathologic specimens were examined by John B. Hazard, M.D., Pathologist, Cleveland Clinic Hospital.

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and apparently extend through the capsule, and that the cells may show mitotic figures, metastases and true malignancy are rare. Duff[7] reviewed 12 cases of islet-cell carcinoma; Frantz[2] reviewed 26 cases considered to be malignant.

Because an islet-cell adenoma rarely causes duodenal obstruction, we present the following unusual case report.

CASE REPORT

Clinical Features.—A 74-year-old woman complained of diarrhea, burning in the stomach, asthenia, and loss of eighteen pounds; these symptoms had been present for four months. The bowel movements were loose and averaged five to six per day; there was considerable mucus in the stools but no blood. The epigastric burning was "ulcerlike" in type, occurring one to two hours after meals and was relieved by food, milk, and alkalies. The weakness and loss of weight were the patient's principal concern. The past history was satisfactory and there were no symptoms suggestive of hypoglycemia.

Fig. 1.—Roentgenogram of stomach showing large dilated atonic duodenal bulb.

There were no significant physical observations.

The hemoglobin was 14.5 Gm., the urinalysis was normal, as were the Wassermann and Kahn tests. Fasting blood sugar was 107 mg. per 100 ml., blood urea was 42 mg. per 100 ml., and blood amylase was 220 units. The Ewald test meal revealed 94 units of free HCl and 106 units of total acidity. Examination of the stool did not disclose occult blood or parasites. Bromsulfalein liver function test was normal.

A roentgenogram of the stomach was normal, but revealed a large and dilated duodenal cap. Subsequent roentgenograms of the stomach continued to show the large and atonic duodenal cap.

The patient was placed on a supportive program with large amounts of vitamins, antiacids because of the epigastric burning and the high acid concentration found on the Ewald test meal, and a high protein diet with frequent feedings. She returned three weeks later to enter the hospital, the symptoms persisting and weight remaining stationary.

The roentgenogram of the stomach was repeated and showed the same dilated duodenal bulb.

In differential diagnosis, an intrinsic lesion of the duodenum such as an old ulcer of the second part of the duodenum or a primary carcinoma of the same area could produce this condition. However, there was no evidence of a crater or of an intrinsic lesion of the duodenum on the barium studies. Moreover, an extrinsic lesion causing pressure and consequent obstruction of the duodenum might have been the causative factor. Such an extrinsic lesion could be an annular pancreas, an aberrant panceas, a pancreatic cyst, a fibrosing type of pancreatitis, a lymphosarcoma, or finally carcinoma of the pancreas. Because of the age of the patient, and because many of the clinical features were suggestive, a preoperative diagnosis of carcinoma of the pancreas was made.

Surgery.—The abdomen was entered through an upper midline incision. In the head of the pancreas there was a well-encapsulated, firm tumor, approximately three inches in diameter which lay within the loop of the second portion of the duodenum in the lesser peritoneal sac. The tumor was attached to the portal vein but not to the common bile duct. The division between the tumor and normal pancreatic tissue was sharp and the mass was freely movable in all directions.

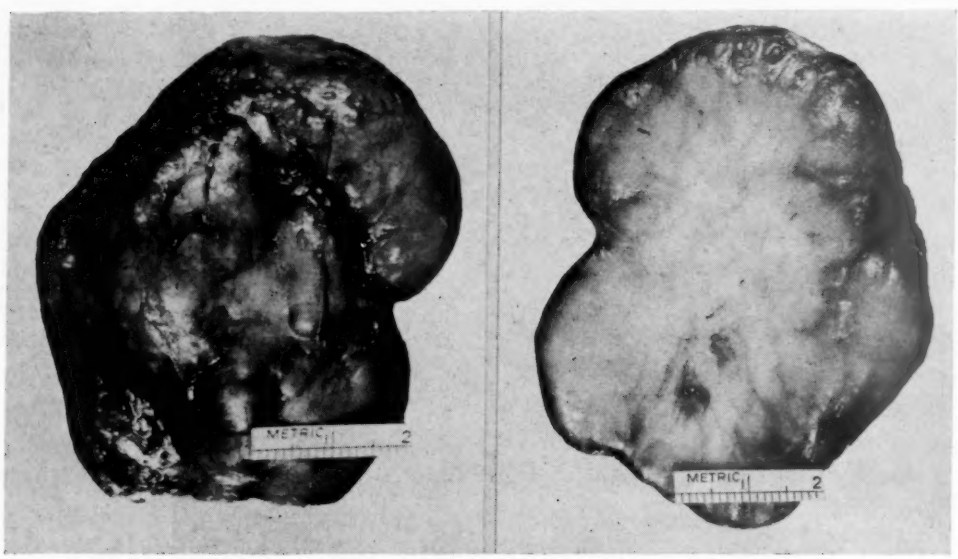

Fig. 2.—Uncut and cut sections of gross tumor removed from head of pancreas.

The lesser peritoneal sac was entered caudad to the pylorus. The tumor was then lifted in the incision and by sharp dissection freed from the second portion of the duodenum. The dissection was carried down posteriorly where the tumor was dissected away from the portal vein and from its attachment to the normal pancreas. The common duct was isolated and the tumor was found to be unattached to it. By blunt and sharp dissection the tumor was completely shelled out of the bed of the pancreas and was removed. During the removal of the tumor there had been some trauma and interference to the blood supply to the second portion of the duodenum; however, it was felt that this segment was viable. The abdomen was closed in the usual way.

Pathology.—The tumor was an irregular round mass of firm light gray-tan tissue with a lobulated surface, covered in all areas by a thin layer of pink, semitranslucent fibrous tissue,

which measured 7 by 5.5 by 5.0 cm. and weighed 78 Gm. The mass cut with resistance to reveal a variegated pattern. Centrally, there was tough, homogenous gray tissue, and peripherally an irregular zone of softer, moist, homogenous light brown tissue. In the intermediate zone, poorly defined bands of firm, white tissue, intermingled with foci of tan tissue, were present. The tumor mass was well defined in all areas from the thin capsular layer of fibrous tissue. No natural pancreatic tissue was identified anywhere in the specimen.

Microscopically, there was a well-encapsulated nodule formed predominantly of polyhedral cells and less numerous elongated cells interspaced between bands of dense collagenous tissue arranged as scattered cords and small masses. Some areas were more cellular. The cells were 10 to 15 microns in diameter and had round to oval nuclei, a few of which were unusually large. The tumor cells had fairly abundant granular cytoplasm and slightly variable nuclei with occasional giant forms; no mitotic figures were seen. Interspersed within the bands of dense collagenous tissue were a few ducts, identical to those of the normal pancreas. No capsular invasion was observed. With Gomori[9] stain (after Zenker-Formol fixation) red-staining granules were seen to be present in some of the cells.

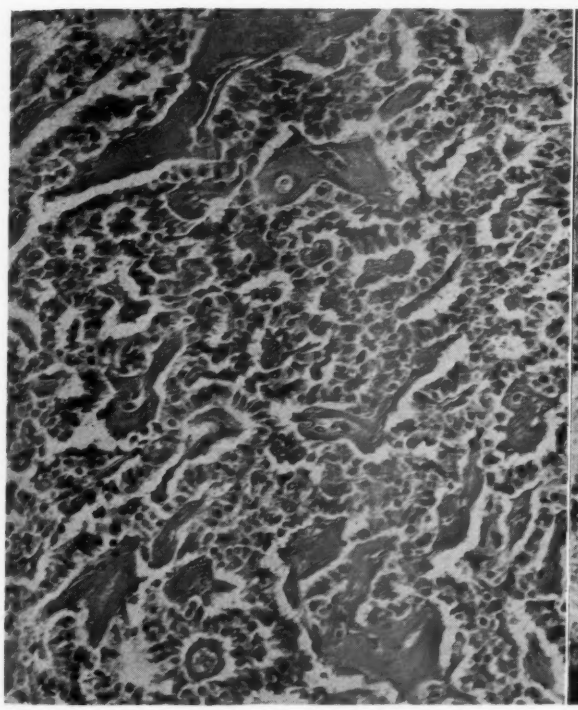

Fig. 3.

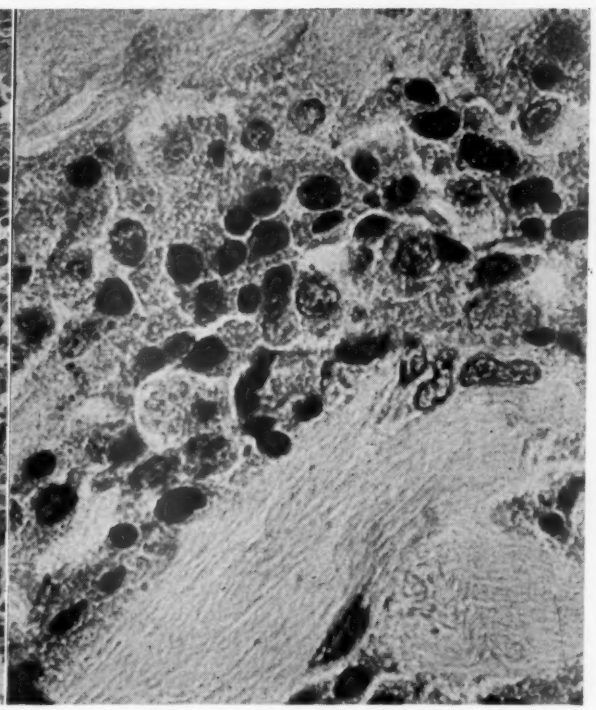

Fig. 4.

Fig. 3.—Microscopic section of tumor showing connective tissue stroma and "duct" formation (×70).

Fig. 4.—Microscopic section of tumor showing granules present in some of cells (×700).

Postoperative Course.—Postoperatively, the patient's appetite returned promptly, the epigastric distress was no longer present, and she experienced no further diarrhea. She was discharged from the hospital seven days after operation. Six weeks later a communication stated that she had gained eight pounds and had developed an excellent appetite. She had had no further epigastric burning and no diarrhea. The patient expressed satisfaction at her complete recovery. One year later she was still in excellent health, and had gained twenty-eight pounds.

DISCUSSION

The case reported is unusual in that the tumor was large, it was located in the head of the pancreas, and it caused symptoms of duodenal obstruction.

Because these tumors are usually in the body or tail of the pancreas (75 per cent), and frequently are small, they rarely produce obstructive (biliary or gastrointestinal) signs or other symptoms due to the size or pressure of the tumor or neighboring organs.

It has been estimated that islet-cell adenomas produce symptoms of hypoglycemia in only about 20 per cent of the cases. Hypoglycemic symptoms are rarely present in patients over 60 years of age. Consequently, it is not surprising that this patient had no symptoms of hypoglycemia.

This pancreatic adenoma was also unusual in that alpha granules were shown to be present in some of the cells by Gomori stain.

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FATALITY AFTER ABDOMINAL ARTERIOGRAPHY

Prevention by New Modification of Technique

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ROENTGENOLOGIC delineation of the abdominal aorta and its branches in human beings after direct translumbar injection of radiopaque medium is an exacting procedure which at present is still in the developmental stage. Indications for abdominal arteriography[1-3] in certain cases of aneurysm, aortic occlusion, hypertension, abdominal tumors, and peripheral vascular disease, as well as recent advances in vascular surgical technique, promise a growing importance in the study and treatment of these conditions. In our series of fifty abdominal arteriographies there was a fatality attributable to an error in technique. It is the purpose of this paper to report the case briefly and to present a modification of technique designed to minimize the dangers of such an error.

CASE REPORT

C. W., a white woman, aged 41 years, was admitted to the Jefferson Hospital on Jan. 31, 1948. The patient was known to have had essential hypertension since the age of 18. She had five previous admissions to Jefferson Hospital because of headaches, dyspnea on exertion, cough, cardiac palpitation, and angina. The case was studied extensively in the medical department and she was also seen in consultation by members of the urologic, endocrinologic, ophthalmologic, peripheral vascular, neurologic, and psychiatric departments. The diagnosis was established as hypertensive cardiovascular disease with arteriolosclerosis and conversion hysteria. The patient's father had died at 53 years of age of coronary artery disease; her brother was suffering from heart disease; and one sister had recently suffered an attack of cerebral apoplexy as well as detachment of the retina.

The patient was severely sick on admission to the hospital. She was cyanotic, moderately dyspneic, and the effort of cooperating for physical examination caused her to perspire profusely. The temperature was normal, pulse rate 120, respirations 24, and blood pressure 166 systolic and 130 diastolic. The heart was enlarged to the left, but no other gross abnormalities were noted. The blood and urine were normal. Roentgenogram of the chest showed great enlargement of the heart to the left with a boot-shaped contour, slight congestion of the lungs, and lengthening with uncoiling of the aorta. The electrocardiogram, in comparison with ones made previously, indicated increase in the degree of left ventricular strain, auricular enlargement, and coronary artery disease.

The patient was kept comfortable with sedatives, opiates, antispasmodics, and oxygen as needed. Since all previous studies of the kidneys had been normal, it was thought to be of some importance, in view of the progressive vascular disease, to visualize the renal arteries and their branches by abdominal arteriography. It was hoped that information regarding the cause of the hypertension might be gained.

Translumbar abdominal arteriography was performed at 9:50 A.M. on Feb. 5, 1948, with the patient under sodium pentothal anesthesia given intravenously. The needle was introduced through the skin about 8 cm. to the left of the midline posteriorly and 3 cm. below the twelfth rib. Arterial puncture was accomplished readily, and the trial injections with physiologic solution of sodium chloride were deemed satisfactory. Ten cubic centi-

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meters of 80 per cent solution of sodium iodide were then injected within five seconds and the roentgenogram was made at the exact conclusion of injection. The anesthetic was administered for three minutes (total dose ¼ Gm.) and the arteriographic technique itself required two minutes.

Wet plate reading of the arteriogram revealed that the needle had engaged the orifice of the superior mesenteric artery. The iodide solution was distributed entirely throughout this vessel and its branches (Fig. 1).

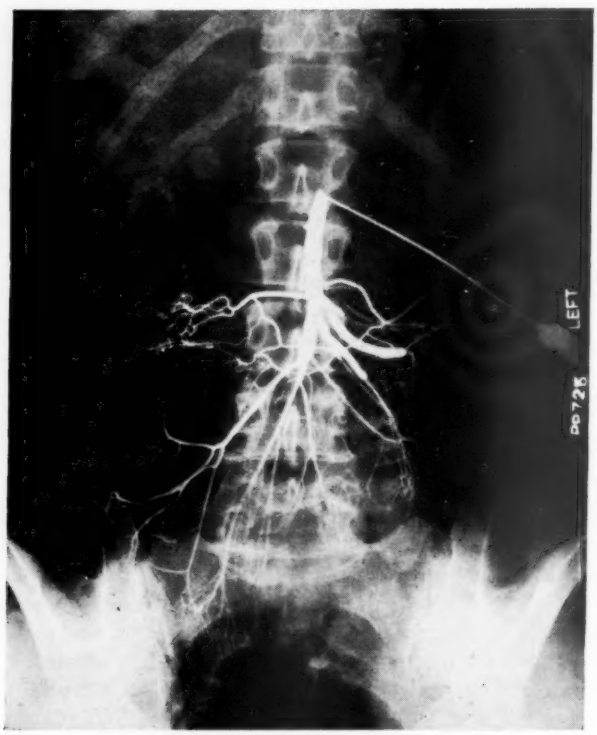

Fig. 1.—Attempted aortography with 80 per cent sodium iodide, showing accidental entrance of needle into orifice of superior mesenteric artery. Death occurred seven hours later, probably due to mesenteric thrombosis.

The patient recovered promptly from anesthesia, but immediately complained of constant diffuse abdominal pain. She was given 50 mg. of demerol hypodermically, and a slow intravenous drip of physiologic solution of sodium chloride was started to hasten the excretion of the iodide. Because of persistent abdominal pain, papaverine hydrochloride, 0.06 Gm., was administered at 11:30 A.M. and demerol 50 mg. at 12:45. At 2 P.M. the abdomen was diffusely tender and rigid, temperature was 97° F., but pulse rate and blood pressure were normal. She was given oxygen by mask. At 4 P.M. she was in profound shock, with restlessness, dyspnea, rapid feeble pulse, temperature 95° F., and unobtainable blood pressure. Despite administration of concentrated plasma, fluids, and oxygen, the patient became increasingly cyanotic, vomited once, and stopped breathing. She was pronounced dead at 4:40 P.M., approximately seven hours after the onset of the abdominal catastrophe.

The patient's death was ascribed to mesenteric thrombosis. Permission for postmortem examination could not be obtained.

NEW MODIFICATION OF TECHNIQUE

Because of the experience cited, we felt that for all subsequent abdominal arteriographies it would be imperative to know the exact position of the needle

before delivering the full dose of radiopaque medium (10 c.c. of 80 per cent sodium iodide). It was found that 10 c.c. of 30 per cent sodium iodide gave adequate visualization for this purpose (Fig. 2). The aortography needle is left in place during the few minutes required to develop the preliminary roentgenogram. Alternate injection of normal saline solution and withdrawal of blood are performed to give assurance that the needle has been maintained in the correct position. If the roentgenogram of the preliminary injection reveals the needle to be in the desired location, and if puncture has been satisfactorily maintained, the 80 per cent solution is injected and the regular aortogram made as in our previous reports.[1, 3] If, on the other hand, the needle is not located so as to visualize the vessels of greatest interest or is located by accident in a

Fig. 2.—Preliminary aortogram with 30 per cent sodium iodide (modified technique), showing accidental entrance of needle into left renal artery. No untoward reaction. The patient had a previous right nephrectomy.

branch (Fig. 2), it is withdrawn. Aortography may then be repeated after an interval of several days. In some instances the vessels in the preliminary aortogram are sufficiently well visualized to obviate the necessity for a second injection with more concentrated solution.

COMMENT

In this patient, correlation of the arteriogram with the subsequent abdominal catastrophe strongly suggested that death was caused by mesenteric thrombosis. The patient may have developed mesenteric thrombosis without the insult of puncture and injection of the mesenteric artery with an irritating

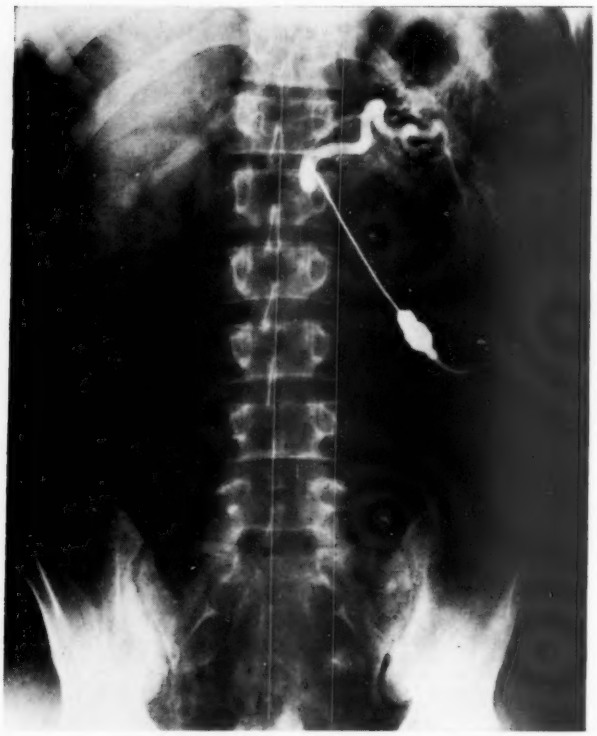

Fig. 3.—Attempted aortography with 80 per cent sodium iodide, showing accidental entrance of needle into celiac axis. Fortunately, no untoward reaction occurred.

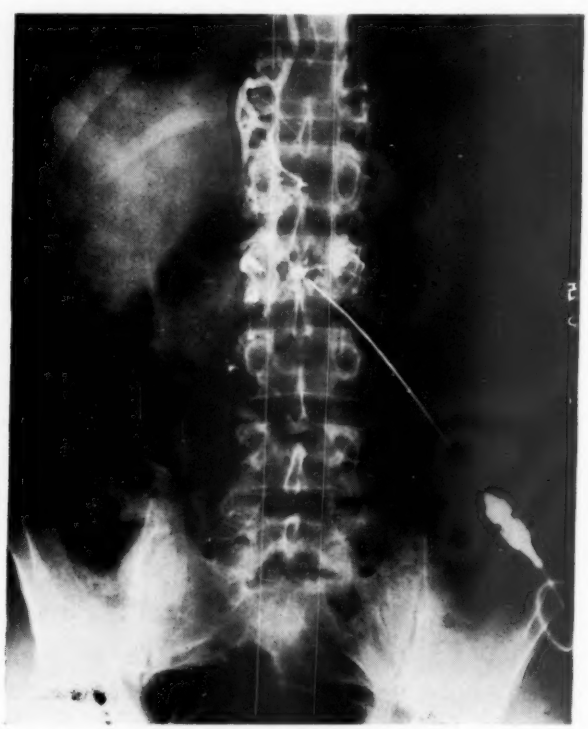

Fig. 4.—Attempted aortography with 80 per cent sodium iodide, showing accidental entrance of needle into azygos system of veins. Fortunately, no untoward reaction occurred.

solution. It is well known that trauma to an artery as the result of puncture by the needle and the force of injection by arterial distention may in themselves provoke reflex vasoconstriction.[4] We believe that this spasm together with the irritating effect of the concentrated iodide solution on the endothelium caused a diffuse thrombosis.

This is the first known report of a fatality following abdominal arteriography. Dos Santos,[5] the originator of this procedure, stated that he performed abdominal arteriography without a single accident in more than 300 human beings; Osario[6] reported approximately 100 aortographies without accident; Nelson,[7, 8] who first reported its use in this country, has performed more than 100 without mention of a death. Doss[9-13] has written extensively on this subject, but gives no figures as to the number performed or any complications in his series.

The difficulties and potential dangers of arteriography have been previously discussed.[3, 4] No consideration, however, was given to the possibility that the needle might enter a branch rather than the aorta itself. Under such circumstances the vessel and tissues it supplies would receive a quantity and concentration of iodide solution much greater than intended. That accidental entrance of some vessel other than the aorta may occasionally take place is demonstrated not only by the case reported (Fig. 1), but in three others from our series (Figs. 2, 3, and 4). Fortunately, in the latter three, no untoward effects were noted. It is, therefore, self-evident that knowledge of the exact position of the needle prior to injection of the full dose of radiopaque medium is essential to the safety of the patient as well as the success of abdominal arteriography.

SUMMARY

1. In our series of fifty abdominal arteriographies, a fatality occurred probably as the result of mesenteric thrombosis. In this patient, who was a poor risk with hypertension and cardiac failure, the needle accidentally entered the orifice of the superior mesenteric artery, which received the iodide solution intended mainly for the abdominal aorta.

2. Abdominal arteriography with 80 per cent sodium iodide solution should be performed only when the exact position of the needle has been determined by preliminary injection with a 30 per cent solution, the technique of which is herein described.

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Editorial

Extension of Radicalism in the Surgical Attack on Cancer

ABOUT the only type of "radical" who seems to be achieving increasing popularity in this country today is the radical cancer surgeon. The extension of the limits of resectability of cancer has occurred *pari passu* with advances in the physiologic management of patients subjected to severely traumatizing procedures. With the brain and the chest now fully accessible to the surgeon, there remain virtually no anatomic frontiers which have not been extensively explored. The improvement in techniques of plastic surgery, substantially accelerated during World War II, has contributed much toward extending the scope of humane surgery in the management of cancers of the mouth and jaws.

The only surgically inviolable structures within the abdominal cavity are two of the branches of the celiac axis—the superior mesenteric and hepatic arteries—and conceivably the time is not far distant when satisfactory artificial replacements for segments of these vessels will be found. Therefore, the surgeon no longer necessarily limits himself to removal of the organ primarily involved in the tumor; he may carry out a block removal of portions of adjacent organs and tissues into which the growth has made direct extensions. Dr. Alexander Brunschwig has pioneered in demonstrating the feasibility of this method of attack. It is true that up until this time these ultraradical procedures have been undertaken mainly to achieve palliation, and less often with the hope that the patient will be permanently cured of cancer. Frequently, the resort to very radical surgery is made only after failure of a primary procedure which has been proved inadequate by recurrence of the disease; by this time the best opportunity for cure has already been lost.

The research opportunity in ultraradical surgery lies in the application of this approach to the *primary* treatment of visceral cancers of types which now show poor results when subjected only to orthodox and limited procedures. We will gain more good for the greatest number by adhering to the rule of "big operations for small cancers and small operations for big ones." The present study of radical panhysterectomy and complete pelvic dissection for early cases of cancer of the cervix uteri, which is being pursued in several centers, is an excellent illustration of this approach. There is reason to believe that a similar opportunity may be provided in improving surgical treatment of cancer of the stomach. Right now this is certainly one of the most discouraging problems we are up against, since out of every hundred patients presenting themselves today for treatment of this disease, the number likely to be alive five years hence will be barely more than can be numbered on the fingers of one hand.

Perhaps this number can be improved by working out mass methods for screening out early and curable cancers from the still asymptomatic population, but no practical test has yet been devised which clearly offers hope of substantial gain by this approach. The material for immediate surgical research in stomach cancer is provided by those cases which now appear at operation to have readily resectable lesions—where the disease appears to be confined to the stomach itself and yet where experience shows there is at best a 25 per cent chance of cure through the types of operations which we have been doing in the past. There is need to determine in a large enough series whether resort to total gastrectomy should be made in larger proportion of cases—whether in antral lesions the partial gastrectomy should be combined with removal of the duodenum and portions of the pancreas and transverse colon. Justification for "compound resections" of this nature in early cases would lie not so much in the expectation of removing unrecognized extensions of the tumor to these adjacent viscera as in gaining the advantage which wide block removal of the related lymphatic drainage areas would provide—areas which cannot now be removed because they also contain the vascular supply to structures usually left behind. Similar approaches are needed for cancer of the bladder and prostate, and, to a lesser degree, for the colon and rectum. The present trend toward performing less radical operations in cancer of the lower rectum, in order to preserve a perineal sphincter, would seem from our own experience to be unjustified and to represent an unwarranted reversal of the desirable trend toward more radical surgery in cancer. Furthermore, in standard operations for breast cancer, there should be less concern for numbers and speed and more concern for performing the sort of operation which will exclude the possibility of local recurrence in the scar.

This type of research must be conducted in the larger teaching centers; only in such places is there the essential coexistence of clinical material, technical specialization of professional staff, trained assistants, laboratory support, and comprehensive follow-up.

Even the most optimistic surgeon must admit, however, that carrying radicalism in surgery to the fullest development possible will still leave us with many incurable cases. In a sense we are trying to make gains on one front, while knowing full well the war on cancer cannot be won until the "second front" gets firmly established, namely, the campaign which attacks the disease with weapons aimed at its cause. Therefore, the surgeon accepts the present necessity of destructive and mutilating operations but looks hopefully toward a future when rational and selective techniques for the prevention and treatment of malignant disease may be provided through contributions of fundamental research. The field of activity of the surgeon has already been drastically altered during the last decade by the marked reduction in the incidence and severity of infections; we would be entirely content if discoveries of the next decade or two should justify complete abandonment of the "surgical front" in the war against cancer.

—John S. Lockwood, M. D.

Recent Advances in Surgery

Conducted by Alfred Blalock, M.D.

VII. THE GENERAL PATHOLOGY OF TRAUMATIC SHOCK

Tracy B. Mallory, M.D., Eugene R. Sullivan, M.D., Charles H. Burnett, M.D., Fiorindo A. Simeone, M.D., Seymour L. Shapiro, B.S., and Henry K. Beecher, M.D., Boston, Mass.

SEVERAL conditions must be satisfied if a relationship between a parenchymal degenerative change or pattern of changes and the clinical state of shock is to be demonstrated. First, the lesions must be sufficiently distinctive, so that there can be no possibility of confusion with post-mortem degeneration or the artefacts of poor fixation and faulty histologic technique. Second, they must be clearly distinguishable from the group of agonal changes seen in the tissues of any individual whose death has not been instantaneous or at least relatively rapid. Specificity of individual lesion cannot reasonably be expected, but the changes should be demonstrable in a high proportion of shock cases, absent in cases of sudden death, and relatively infrequent in cardiac, metabolic, or cerebral deaths in which shocklike states are comparatively uncommon. There should be a demonstrable time relationship between the onset of shock and appearance of the lesions, and conversely between recovery from shock and their disappearance. So far as could be ascertained, no pattern of lesions which fulfills these conditions[1, 2] in man has been described.

The anatomic changes associated with shock may be usefully divided into (1) those which occur concomitantly with the state of shock and therefore are of interest in relation to its pathogenesis, and (2) those which follow shock and therefore may be considered as its consequences. In studies of the pathology of human shock, attention has heretofore been concentrated primarily on the former. In the present work, attention is devoted particularly to the latter; but two brief sections dealing with pulmonary edema and with fat embolism have been included because of the extensive consideration given to them by previous investigators.

In our own preliminary investigations, the search for possible sequelae of shock seemed fruitless for many months. The post-mortem material of several hundred battle casualties was vainly examined for any lesion or combination of lesions which would fulfill the imposed conditions. The organs of patients dying after four, eight, or twelve hours of prolonged shock showed little evidence of histologic change and none which could not be duplicated readily in a series of nonshock cases. When, however, the range of investigation was broadened to include material from casualties who lived more than eighteen hours after injury, and when frozen sections stained for fat with sudan IV were substituted for paraffin sections, a fairly constant pattern was disclosed.

Evidence was obtained that approximately eighteen hours after a shock-producing injury, fat vacuolation appears in the parenchymal cells of the heart, liver, and kidneys. These changes increase in frequency and severity up to ninety-six hours after injury, then progressively decline with longer periods of convalescence from the episode of shock, unless complicating factors, such as fat embolism or severe infection, prevent resolution of the process.

The pancreas and adrenal gland were also studied in the same group of cases. In the pancreas no lesion was recognized which appeared to correlate with shock. In the adrenal gland a series of changes was readily demonstrable: swelling of the cortex, pseudotubular degeneration, and depletion of stainable lipid, particularly of doubly refractile lipid. Since these changes are less marked quantitatively and do not differ qualitatively from those seen in cases with infection and in other types of control material, their significance is questionable. Only one factor, the depletion of doubly refractile lipid elements, showed a tendency to reversibility with increasing time intervals following resuscitation from shock.

MATERIAL

The nucleus of material for this section of the report was provided by the necropsy protocols and corresponding microscopic preparations from sixty cases which had been studied clinically by members of the Board.* As the work progressed, the importance of sepsis as a complicating factor became apparent. Additional cases were therefore selected from the files of the Fifteenth Medical General Laboratory in which the clinical data were sufficiently detailed to establish the diagnosis of shock and in which major sepsis could be excluded. Numerous additional examples of acute shock were included in order to cover a wider time range than was provided by the Board's cases. Control material was drawn both from the Fifteenth Laboratory and from the Army Institute of Pathology.

The majority of necropsies were performed under field conditions by an officer of a Field or Evacuation Hospital whose experience in pathology was often limited. (In the original sixty cases, one of the Board members usually was present at the necropsy.) Deaths were most numerous at times of heightened military activity when hospital staffs were overworked in caring for the living. Necropsies were sometimes conducted in hospital operating rooms, but more often in tents without benefit of flooring, heat, or adequate illumination. Scales were rarely available. The examinations and records were inevitably incomplete. The central nervous system was rarely examined, the intestinal tract seldom opened, and wounds of the extremities were given but cursory attention to determine the presence or absence of gross infection, major vascular involvement, or extensive necrosis of muscle. Blocks of representative tissues were fixed in formalin, occasionally in Zenker's solution, and transmitted to the pathology section of the Fifteenth Medical General Laboratory, where they were sectioned and the histologic findings were reviewed (by T. B. M.).

*Board for the Study of the Severely Wounded, Mediterranean Theater of Operations, United States Army.

FINDINGS

Lungs

The Board's cases include no examples of sudden death; hence the lungs were never normal. Congestion was described in every case: edema in approximately 85 per cent; atelectasis in 70 per cent; fat embolism in 65 per cent; intra-alveolar hemorrhage in 55 per cent; interstitial hemorrhage in 25 per cent; and pneumonia in 30 per cent. Because two of these lesions, pulmonary edema and fat embolism, have received considerable attention in relation to the mechanism of shock, their significance is worth examining in more detail.

Pulmonary Edema.—Estimation of the severity of pulmonary edema is difficult from the available data in view of the large number of prosectors and the few lung weights recorded. A rough classification into three grades has been attempted: Grade I, little or no edema (classified as "slight") with lung weights probably below 800 Gm.; Grade II, moderate edema with lung weights between 800 and 1,200 Gm.; and Grade III, severe edema with lung weights from 1,200 to 1,800 Gm. Seventeen cases were Grade I (slight), sixteen Grade II (moderate), and twenty Grade III (severe).

Several factors might influence the development of pulmonary edema in these patients. It has been suggested[2] that pulmonary edema is a constant and integral part of the shock mechanism. It is certainly a common sequela of renal insufficiency, from which a large proportion of the patients in this series suffered. It could be due to myocardial failure, and evidence will be presented later in this paper that myocardial degeneration actually was present in many cases. It might be influenced by fat embolism, and finally it could be brought about, or at least intensified, by overenthusiastic intravenous fluid therapy.

In Table I the degree of pulmonary edema is compared with the period of survival from injury to death in forty-seven shock cases. In all tables in this paper the figures represent the number of cases falling in each category. The patients dying in less than forty-eight hours represent by and large the group in which resuscitation was unsuccessful. One patient (Case 22)* briefly appeared to be resuscitated, only to develop two secondary attacks of circulatory failure, from the second of which he died. These patients may fairly be considered

TABLE I. SEVERITY OF PULMONARY EDEMA AND SURVIVAL PERIOD (FORTY-SEVEN SHOCK CASES)

PULMONARY EDEMA	SURVIVAL PERIOD (NUMBER OF CASES)			
	LESS THAN 48 HOURS	3 OR 4 DAYS	MORE THAN 4 DAYS	
			UREMIC	NONUREMIC
Grade I (slight)	5	3	4	3
Grade II (moderate)	2	2	6	4
Grade III (severe)	3	7	7	1

*Our original case numbers are retained in the hope that eventually The Surgeon General will make this source material generally available for reference and in order to facilitate correspondence that may grow out of the publication of this series of articles.

to have died in, perhaps of, severe and prolonged shock. Five had minimal, two moderate, and only three severe edema. All had received repeated infusions of plasma and whole blood.

In the patients who survived into the third or fourth days, it is safe to assume that shock had disappeared. In the majority of these, incipient renal insufficiency was manifest and only one patient failed to show a nephropathy at post-mortem examination. They were oliguric or anuric, and the plasma nonprotein nitrogen had climbed to levels of from 90 to 130 mg. per 100 c.c., though few or no symptoms of uremia were present. In nine of these cases there was a moderate or severe pulmonary edema, but since in five of them there was also histologic evidence of myocardial degeneration, it would be impossible to assess the relative importance of cardiac and renal factors.

The twenty-five patients who died on the fourth day or later were divided into uremic and nonuremic groups. Pulmonary edema of moderate or severe degree was present in thirteen of the seventeen patients in the former group, despite the fact that many of these patients were treated in consultation with clinical members of the Board and the intake of fluid was rigidly restricted. Since there was histologic evidence of myocardial injury in only three patients of this group, the evidence points strongly to renal insufficiency as the primary cause of the pulmonary edema. In the nonuremic group the most frequent cause of death was peritonitis. Only one of these eight patients showed severe edema.

In summary, pulmonary edema was less frequent and less severe in patients who were never successfully resuscitated from shock than in those patients who did recover from the acute stage of shock but developed evidence of renal insufficiency. Our anatomic data offer no confirmation for the hypothesis that loss of fluid into the alveoli is an important factor in the development of shock.

Pulmonary Fat Embolism.—Pulmonary fat embolism is a very frequent complication of battle casualties, as the 65 per cent incidence in the present group of patients shows. Its significance is extremely difficult to assess. In the early stages of World War I much attention was given to it, and it was considered by some investigators[3] to be an important, perhaps the most important, cause of shock. Further experience failed entirely to substantiate the hypothesis, the theories of Bayliss and Cannon[4] became dominant, and fat embolism was forgotten.

Frozen sections were cut and stained for fat in all of the present series of cases in which lung tissue was available (fifty-one cases). An attempt was made to estimate the severity of the embolism in three grades as follows: In Grade I only an occasional droplet is seen. In Grade II droplets are fairly numerous; they are found chiefly in large vessels or arterioles and seldom have passed into the capillaries of the alveolar walls. In Grade III a considerable proportion, one-quarter to one-half or more, of the arterioles are plugged, and in numerous areas capillaries are filled as if by an injection mass. Systemic fat embolism of significant grade was never found in association with Grades I and II, but was present in about one-fifth of the cases in Grade III. Judging by

TABLE II. FAT EMBOLISM AND SHOCK (FIFTY-ONE CASES)

DEGREE OF SHOCK	GRADE OF FAT EMBOLISM (NUMBER OF CASES)				
	0	I	II	III	TOTAL CASES
None	5	--	2	--	7
Slight	1	2	--	2	5
Moderate	3	3	2	3	11
Severe	8	11	4	5	28
Total	17	16	8	10	51

experience covering several hundred battle casualties, we considered it improbable that Grades I and II of pulmonary fat embolism are functionally significant.

In Table II the grade of fat embolism is compared with the degree of shock. It is apparent from inspection of the table that Grade III fat embolism was present in only eight of the thirty-nine cases of moderately severe or severe shock. Conversely, of ten patients with significant fat embolism, eight were estimated to have moderate or severe shock. It is evident that fat embolism is not the cause of shock in any considerable proportion of patients. Severe pulmonary fat embolism was always associated with shock, usually of moderate or severe degree. To determine whether or not this relationship is causal would require the study of a much larger series of cases than the present one.

TABLE III. FAT EMBOLISM AND PULMONARY EDEMA (FORTY-FOUR CASES)

DEGREE OF PULMONARY EDEMA	GRADE OF FAT EMBOLISM (NUMBER OF CASES)			
	0	I	II	III
Slight	5	5	1	3
Moderate	5	5	2	2
Severe	4	4	4	4

Fat Embolism and Pulmonary Edema.—In Table III the grade of pulmonary fat embolism is compared with the degree of pulmonary edema. It is obvious that there is no correlation.

Heart

Material was available from forty-four of the Board cases and from sixty-one of the supplemental series. Abnormal fat vacuolation was found in twenty-four cases. This consisted of very minute vacuoles, seldom more than 2 microns in diameter, arranged in parallel rows between the myofibrils. When present in a cell, the vacuolation was apparent throughout the cell's entire length and breadth, rarely segmentally or focally. It was entirely independent of the amount of lipochrome demonstrable at the nuclear poles. The affected cell often seemed slightly swollen in the frozen section, but this change could not be recognized with certainty in the paraffin sections. Sometimes single cells, more often groups of from ten to fifty adjacent fibers, were affected. Vacuolation was never diffuse throughout the myocardium. In appearance it was strongly reminiscent of, though usually less severe than, the patchy fat vacuolation seen in severe anemia. However, no gross changes suggestive of tigering were ever noted.

TABLE IV. MYOCARDIAL FAT VACUOLATION IN SHOCK CASES (FIFTY-FIVE CASES)

GRADE OF FAT VACUOLATION	SURVIVAL PERIOD (NUMBER OF CASES)		
	LESS THAN 18 HOURS	18 TO 96 HOURS	MORE THAN 4 DAYS
0	10	4	24
1+	0	4	2
2+	0	2	3
3+	0	6	0
Percentage of cases positive	0	75	17

The severity of the change, estimated by the number and size of the vacuoles per cell and the proportion of cells involved, was roughly quantitated on a 0-to-3+ scale. The degree of involvement is compared with the survival period in Table IV.

It is evident that fat vacuolation of cardiac muscle cells was not observed in previously healthy young men who developed shock following trauma but failed to survive at least eighteen hours. In patients manifesting shock who lived from eighteen to ninety-six hours, fat vacuolation of the myocardium was found in 75 per cent. With longer periods of survival the incidence dropped sharply to 17 per cent, and there were no cases of grade 3 + severity.

Focal fat vacuolation of cardiac muscle cells has been noted frequently (by T. B. M.) in cases of systemic fat embolism with embolization of the myocardial capillaries. In only two of the group under consideration was this complication present. These two men died on the fifth and sixth days after injury. If they are excluded, the incidence of fat vacuolation in the patients surviving more than four days falls to 11 per cent.

TABLE V. DEGREE OF SHOCK AND FAT VACUOLATION OF MYOCARDIUM IN FOURTEEN PATIENTS WHO SURVIVED FROM EIGHTEEN TO NINETY-SIX HOURS

DEGREE OF SHOCK	GRADE OF FAT VACUOLATION (NUMBER OF CASES)			
	0	1+	2+	3+
Slight	0	0	1	0
Moderate	1	2	1	1
Severe	2	1	0	5

In Table V the fourteen patients who died within the eighteen to ninety-six hour period and who had been examined during life by a clinical member of the Board are tabulated according to the degree of shock and the severity of the fat vacuolation. The number of cases is small, but increasing intensity of fat vacuolation is apparent as shock becomes more severe.

TABLE VI. FAT VACUOLATION OF MYOCARDIUM IN FIFTY-ONE CONTROL CASES

NUMBER OF CASES	TYPE OF CASE	GRADE OF FAT VACUOLATION (NUMBER OF CASES)				PER CENT POSITIVE
		0	1+	2+	3+	
15	Sudden deaths	15	0	0	0	0
12	Starvation deaths	12	0	0	0	0
9	Deaths from aplastic anemia	6	0	2	1	33
15	"Medical" deaths	11	2	1	1	27

Control Cases.—In Table VI a group of fifty-one control cases is listed. These include a number of instances of sudden death and a miscellaneous group of medical conditions. Since fat vacuolation can be produced in experimental animals by short periods of starvation,[5] it seemed appropriate to study some cases of death by starvation in prison camps. And, as fatty change in the myocardium has long been recognized as a sequela of severe anemia, a series of cases of aplastic anemia was included. Analysis of the material from the point of view of the presence or absence of peritonitis, an important factor in relation to liver and adrenal lesions, yielded no evidence that infection was important in the production of the myocardial changes.

Summary.—Fat vacuolation of cardiac muscle fibers is a pathologic process not seen in previously healthy persons who die suddenly or who die following a shock-producing injury in a period of less than eighteen hours. It is found in 75 per cent of individuals who have survived a similar injury for periods of eighteen to ninety-six hours, but becomes unusual in those living more than four days after injury. In a small sample group the degree of fatty change appeared to parallel the severity of shock. Though the lesion is found inconstantly in a variety of medical conditions, particularly those associated with severe grades of anoxemia, the frequency is considerably below that observed following shock.

Liver

Fat vacuolation of the liver appears in such a variety of conditions and may be present in so many apparently normal individuals that there is often a temptation to regard it as not significant, unless the amount is very great. The usual form observed consists of vacuoles of considerable size, ranging from 5 to 20 microns in diameter. Such vacuoles are readily visible in paraffin sections with low magnification (16 to 30 mm. objectives) inasmuch as they occupy the full thickness of the section and appear as sharply outlined holes. Because of their large size there are never many vacuoles in a single cell.

Fat vacuolation of this type is rarely seen in shock cases, and when found probably existed before the shock-producing injury. Extensive fat vacuolation is nevertheless readily demonstrable in shock if sufficient time has elapsed for its development. This form of fat vacuolation consists almost entirely of very fine droplets in the range from 2 to 4 microns in diameter. Even when the process is severe, though the droplets may enlarge slightly, there is little tendency for them to fuse, and as many as fifteen or twenty may be present in a single cell. The vacuolation is readily seen in paraffin sections if the 4 mm. lens is used. Few of them extend through the thickness of the section, but two or more layers can be seen by varying the depth of focus. Because of the small size of the vacuoles, some difficulty may be experienced in frozen sections in distinguishing them from the normal pigment which is often slightly sudanophilic. The fat vacuoles are a little larger than the pigment granules and are rounder. Very often they show a crescentic intensification of the stain on one margin.

The affected cells in the initial stages are always centrally located in the lobule; with increasing severity the involvement spreads to the periphery.

There is little evidence of swelling of the cells, and the organ as a whole is not enlarged, yellow, or greasy. For this reason it seems improbable that the amount of fat in the liver can have been greatly increased, though a check by chemical methods would be necessary to decide this issue.

The occurrence of small-droplet fat in relation to the survival period in fifty-one Board cases is shown in Table VII. It is evident that in shock patients surviving from eighteen to ninety-six hours, moderate to severe fat vacuolation was an almost constant finding. With longer survival periods, the proportion of cases with mild or no fat vacuolation increased progressively, but many instances of severe vacuolation were still found.

TABLE VII. FAT VACUOLATION IN THE LIVER IN FIFTY-ONE BOARD CASES WITH SHOCK

GRADE OF FAT VACUOLATION	SURVIVAL PERIOD (NUMBER OF CASES)	
	18 TO 96 HOURS	MORE THAN 4 DAYS
0	1	12
1+	1	4
2+	3	6
3+	15	9
Percentage of cases grade 2+ or 3+	90	48

In reviewing the group of thirty-one patients who survived more than four days, it became apparent that severe fatty changes were particularly frequent in patients with peritonitis, the only common cause of prolonged sepsis in this series. This is brought out in Table VIII.

TABLE VIII. INFLUENCE OF PERITONITIS UPON FAT VACUOLATION IN LIVER (CASES WITH MORE THAN FOUR DAYS' SURVIVAL PERIODS)

GRADE OF FAT VACUOLATION	PERITONITIS (NUMBER OF CASES)	NO MAJOR INFECTION (NUMBER OF CASES)
0	3	9
1+	1	3
2+	3	4
3+	7	1

Since twenty-six of the Board cases were complicated by peritonitis, the significance of the figures in Table VII is open to doubt. In Table IX, which includes the twenty-eight supplementary cases from the Fifteenth Laboratory, all cases of peritonitis or other major sepsis have been excluded. In this selected

TABLE IX. FAT VACUOLATION OF LIVER CELLS IN FIFTY-THREE SHOCK CASES UNCOMPLICATED BY MAJOR INFECTION

GRADE OF FAT VACUOLATION	SURVIVAL PERIOD (NUMBER OF CASES)		
	LESS THAN 18 HOURS	18 TO 96 HOURS	MORE THAN 4 DAYS
0	11	3	9
1+	2	6	3
2+	1	4	4
3+	0	9	1
Total	14	22	17
Percentage of cases positive	22	87	47
Percentage of grade 2+ or 3+	7	60	30

series it is apparent that fat vacuolation of more than minimal degree was seldom seen in shock patients who failed to survive at least eighteen hours. Of those who survived from eighteen to ninety-six hours, 87 per cent showed the presence of fat, 59 per cent in moderate or severe degree. With survival beyond ninety-six hours, the tendency to return to normal is seen, the total dropping to 47 per cent and that for the severer grades to 29 per cent.

Clinical estimates of the severity of shock, as well as tissue for fat stains, were available in seventeen cases from the eighteen to ninety-six hour group. In Table X these features are compared. The apparent parallelism between

TABLE X. FAT VACUOLATION IN THE LIVER RELATED TO DEGREE OF SHOCK (CASES WITH EIGHT TO NINETY-SIX HOURS' SURVIVAL PERIODS)

DEGREE OF SHOCK	GRADE OF FAT VACUOLATION (NUMBER OF CASES)			
	0	1+	2+	3+
Slight	0	0	1	0
Moderate	0	0	1	4
Severe	0	1	2	8

severity of shock and degree of fat vacuolation is questionable because of the presence of a complicating peritonitis in the majority of cases.

Control Cases.—Since fat vacuolation of the liver is such a common phenomenon and can be produced by so many etiological factors, numerous control cases seemed necessary. Seventeen instances of sudden death were selected at random from the laboratory files. Fifteen cases of "medical" deaths without obvious shocklike states (cardiac, cerebral, nephritic), twenty instances of death from aplastic anemia, and thirty-eight deaths from starvation were included, making a total of ninety control cases. The incidence of centrolobular fat vacuolation is shown in Table XI.

TABLE XI. CENTROLOBULAR FAT VACUOLATION OF LIVER

TYPE OF CASE	NUMBER OF CASES	GRADE OF FAT VACUOLATION (NUMBER OF CASES)				PERCENTAGE GRADE 2+ or 3+
		0	1+	2+	3+	
Controls:						
Sudden deaths	17	8	5	2	2	24
"Medical" deaths	15	3	6	3	3	40
Deaths from aplastic anemia	20	10	6	1	3	20
Starvation deaths	38	0	0	0	0	0
Shock cases: less than 18 hours' survival	14	11	2	1	0	7
Shock cases: 18 to 96 hours' survival	22	3	6	4	9	60

The occurrence of moderate or severe fat vacuolation in 24 per cent of the sudden-death group is worthy of comment. This group was compiled largely from motor vehicle accident and homicide cases in base section troops. The proportion of limited service and older men is higher in such troops than in combat organizations. Two of the men in the group studied had been intoxicated at the time of death, and had enlarged, grossly fatty livers suggestive of chronic alcoholism. In contrast, the acute-shock group, with survival periods shorter than eighteen hours, was made up almost entirely of battle casualties,

all previously healthy and vigorous young men, and therefore represents a better control group than the "sudden deaths." The relatively high incidence (40 per cent) in the "medical" deaths is not surprising in view of the multiple etiology of fat deposit in the liver, but it is well below the 60 per cent frequency in the eighteen to ninety-six hour shock group. The low incidence in the anemia group proved surprising in view of the known frequency of myocardial fat vacuolation in such conditions. The starvation cases provided a most interesting contrast to the shock material. Although fat was present in the majority, it was always manifest at the periphery, never at the center of the lobule.

Summary.—Eighteen hours after a shock-producing injury, fat vacuolation was demonstrable in the liver cells at the center of the lobule in 87 per cent of fifty-three cases uncomplicated by major infection, and was of moderate or severe grade in 60 per cent. After the fourth day it tended to disappear in cases uncomplicated by peritonitis. The incidence in the eighteen to ninety-six hour cases was significantly higher than in any of the control groups studied. In a limited number of cases the severity of fat vacuolation appeared to parallel the intensity of shock, but the presence of complicating peritonitis in the majority of these cases renders the significance of this observation doubtful.

Kidney

The histologic changes in the kidney following shock have been described elsewhere in detail.[6] Fat vacuolation in the ascending limb of Henle's loop was shown to be the first definite histologic evidence of renal injury. In the present analysis only this feature of the numerous renal changes which may develop will be considered. Approximately the same supplementary cases have been added to the Board cases as were described in the preceding sections. The findings in ninety cases are summarized in Table XII.

TABLE XII. FAT VACUOLATION OF ASCENDING LIMBS OF HENLE IN NINETY SHOCK CASES

SURVIVAL PERIOD	NUMBER OF CASES	GRADE OF FAT VACUOLATION (NUMBER OF CASES)				PERCENTAGE POSITIVE	PERCENTAGE GRADE 2+ OR 3+
		0	1+	2+	3+		
Less than 18 hours	20	17	2	1	0	15	5
18 to 24 hours	11	5	1	4	1	55	45
24 to 96 hours	26	4	1	4	17	85	81
More than 4 days	33	14	6	7	6	58	39

As in the heart and liver, fat vacuolation was rarely found in shock patients surviving less than eighteen hours after injury. It was already present in 55 per cent of the eighteen to twenty-four hour group and was evident in 85 per cent of those surviving from one to four days. With survival beyond that period it decreased somewhat in frequency to 58 per cent, and considerably in severity, the 2+ and 3+ grades dropping from 81 per cent to 39 per cent. In the kidney, as in the heart, the severity of fat vacuolation was uninfluenced by the presence or absence of peritonitis.

Control Cases.—The degree of fat vacuolation in the ascending limbs of Henle's loop in fifty-five control cases is shown in Table XIII. Fat vacuolation in the ascending limbs is found with sufficient frequency (43 per cent of

TABLE XIII. FAT VACUOLATION OF ASCENDING LIMBS IN FIFTY-FIVE NONSHOCK CASES: CONTROL GROUP

TYPE OF CASE	NUMBER OF CASES	GRADE OF FAT VACUOLATION (NUMBER OF CASES)				PERCENTAGE POSITIVE	PERCENTAGE GRADE 2+ OR 3+
		0	1+	2+	3+		
Sudden deaths	19	19	0	0	0	0	0
"Medical" deaths	14	8	3	1	2	43	22
Starvation deaths	12	8	1	3	0	50	38
Deaths from aplastic anemia	10	8	1	1	0	25	13

the "medical" deaths in the present group) to have led some authors[7] to consider it normal. Its complete absence in nineteen instances of sudden death and its presence in only 15 per cent of twenty shock cases representing patients who died in less than eighteen hours following injury clearly indicate that it is not a normal finding in healthy young men in the eighteen to thirty-five year age group. Dible[8, 9] has shown that fat rapidly appears in this segment of the nephron in starvation experiments in rabbits. The data on starvation deaths included in our series showed an incidence of 50 per cent, with 38 per cent of 2+ or 3+ grade. These figures are nevertheless well below those (85 per cent and 81 per cent) of the one- to four-day shock cases shown in Table XII.

Summary.—Fat vacuolation of the ascending limbs of Henle's loop is abnormal in men from 18 to 35 years of age. It was found in only 15 per cent of shock patients dying in less than eighteen hours but was present in 85 per cent of shock patients surviving from one to four days after injury. From the fourth day onward a decrease in frequency and severity was demonstrable, regardless of whether or not a hemoglobinuric nephrosis developed.

Adrenal

A normal adrenal gland is rarely seen at necropsy by the civilian pathologist who does not have opportunity to perform post-mortem examinations upon individuals who have died suddenly without previous disease. The adrenal gland of the healthy young male has a narrow cortex which ranges from 1.0 to 1.3 mm. in width. The cells are richly packed with lipid (stainable with sudan IV), predominantly in the fascicular layer, but numerous vacuoles are also demonstrable in the zona glomerulosa and reticularis. Limited to the zona fasciculata are large amounts of doubly refractile lipid which serve to outline this layer sharply when viewed with crossed Nicol prisms.

In our shock cases no medullary changes but a variety of cortical changes were observed. The amount of stainable lipid decreased and the optically active fraction was markedly depleted. The cortex was slightly swollen and frequently showed the pseudoacinar type of degeneration described and illustrated by F. B. Mallory in 1914,[10] more recently emphasized by Rich[11] in relation to sepsis, and noted by Mallory and Brickley[12] in the burn victims of the Cocoanut Grove disaster. The changes observed did not differ qualitatively from, and were less severe quantitatively than, those of sepsis or of such control conditions as aplastic anemia and starvation, though some degree of terminal infection may have complicated much of this control material. Only one feature, the doubly

TABLE XIV. STAINABLE LIPIDS IN ADRENAL CORTEX IN FORTY SHOCK CASES WITHOUT SEPSIS AND EIGHTEEN CONTROL CASES

TYPE OF CASE	NUMBER OF CASES	DEGREE OF FAT VACUOLATION (NUMBER OF CASES)				PERCENTAGE DIMINISHED	PERCENTAGE GREATLY DIMINISHED
		3+	2+	1+	0		
Sudden deaths (control cases)	18	18	0	0	0	0	0
Shock (less than 18 hours' survival)	11	11	0	0	0	0	0
Shock (18 to 96 hours' survival)	13	8	3	2	0	38	15
Shock (more than 4 days' survival)	16	4	8	4	0	75	25

refractile lipid depletion, showed evidence of reversibility with recovery from shock. In Tables XIV and XV the stainable and the doubly refractile lipids are compared in a group of forty shock patients free from septic complications and a control group of eighteen sudden deaths. The amount of lipid, as in other organs, was visually estimated on a 0-to-3+ scale. In this instance, however, the maximal 3+ figure represents the normal, and 0 represents the stage of maximal depletion.

A moderate depletion of the total stainable fat is evident in the shock group surviving from eighteen to ninety-six hours. There is no evidence, however, of return to normal with longer intervals of survival after recovery from shock; the process is, in fact, much intensified in the group surviving more than four days.

TABLE XV. DOUBLY REFRACTILE LIPIDS IN ADRENAL CORTEX IN FORTY SHOCK CASES WITHOUT SEPSIS AND EIGHTEEN CONTROL CASES

TYPE OF CASE	NUMBER OF CASES	AMOUNT OF LIPID (NUMBER OF CASES)				PERCENTAGE DIMINISHED	PERCENTAGE GREATLY DIMINISHED
		3+	2+	1+	0		
Sudden deaths (control cases)	18	15	3	0	0	17	0
Shock (less than 18 hours' survival)	11	8	2	1	0	27	9
Shock (18 to 96 hours' survival)	13	1	4	7	1	92	61
Shock (more than 4 days' survival)	16	3	7	3	3	81	38

In contrast to the stainable lipid, the doubly refractile fraction was occasionally below the usual level in cases of sudden death (17 per cent), and was depleted in 27 per cent of shock patients who died in less than eighteen hours; in one case it was severely depleted. In the shock cases of eighteen to ninety-six hours' survival, this type of lipid was diminished in all but one instance (92 per cent of the cases) and markedly so in eight cases, or 61 per cent. In those patients surviving more than four days, some evidence of a tendency to return to normal is shown by a drop in the percentage of severe depletion from 61 to 38 per cent.

Control Material.—It was difficult to know what kind of control material would be suitable, inasmuch as most types of illnesses which lead to death

TABLE XVI. ADRENAL CORTICAL LIPIDS IN FORTY-FOUR CONTROL CASES

TYPE OF CASE	NUMBER OF CASES	STAINABLE FAT		DOUBLY REFRACTILE LIPIDS	
		PERCENTAGE DIMINISHED	PERCENTAGE GREATLY DIMINISHED	PERCENTAGE DIMINISHED	PERCENTAGE GREATLY DIMINISHED
"Medical" deaths	14	50	22	79	29
Starvation deaths	9	78	44	100	78
Deaths from aplastic anemia	11	82	18	91	91
Fatal cases with sepsis	10	100	80	100	100

produce similar and even more marked adrenal changes. Four groups of control cases are listed in Table XVI.

It is evident that a wide variety of factors affects the storage of lipid substances in the adrenal cortex, many of them more influential than shock.

Summary.—Although numerous changes occur in the adrenal cortex following shock, they do not differ in character from, and are less severe than, those seen in infection and in a wide variety of lethal disorders. The only factor which was found to change abruptly eighteen hours after a shock-producing injury was the amount of doubly refractile lipid in the zona fasciculata. This was diminished in 92 per cent of the cases in the eighteen to ninety-six hour group (see Table XV). This factor also was the only one in which any tendency could be established to return toward normal with increasing time intervals following recovery from shock.

COMMENT

The possible roles of pulmonary edema and of fat embolism in the pathogenesis of shock in men wounded in battle have been discussed in the sections devoted to these phenomena. The pattern of parenchymal degenerative changes described in the heart, liver, kidneys, and adrenals deserves further consideration as a probable consequence of shock. None of the changes described is specific for the state of shock. Fat is known to make its appearance in one or another of these organs in response to a variety of pathologic conditions such as anoxemia, starvation, and chemical or bacterial toxic agents, and lipids disappear from the adrenal under an even greater variety of conditions. Critical examination of the data is therefore necessary before concluding that the observed changes are due to shock.

Errors of subjective interpretation in relying upon such vague changes as "parenchymatous degeneration" and "cloudy swelling," which are readily confused with post-mortem degeneration and the artefacts of faulty histologic technique, have been avoided by the use of frozen sections and fat stains; general histologic experience indicates that there is no significant shift in the proportion of stainable fat up to twelve hours after death. Less is known of the behavior of doubly refractile lipids, but in the material included in this study no evidence was discovered that this fraction of the fatty substance was affected by post-mortem degeneration within the same time limit. The observed variations from the normal are therefore vital phenomena.

TABLE XVII. PERCENTAGE OF ABNORMAL FAT CHANGES IN THE HEART, LIVER, KIDNEY, AND ADRENAL IN SHOCK

TYPE OF CASE	HEART (PER CENT)	LIVER (PER CENT)	KIDNEY (PER CENT)	ADRENAL GLAND DEPLETION OF DOUBLY REFRACTILE LIPID (PER CENT)
Sudden deaths (control group)	0	24	0	17
Shock (less than 18 hours' survival)	0	22	15	27
Shock (18 to 96 hours' survival)	75	87	76	92
Shock (more than 4 days' survival)	17	47	58	81

Next in importance are the time relationships to shock. Table XVII shows the percentage of all cases with abnormal fat vacuolation in the heart, liver, and kidney, and depletion of the doubly refractile lipid in the adrenal, for each group and for the sudden-death control group.

In each of the four organs studied no significant difference in demonstrable fat is apparent between the sudden-death series and the shock cases in which death occurred in less than eighteen hours. Abnormal changes are evident, however, in these organs in from 75 to 92 per cent of shock patients who survived from eighteen to ninety-six hours after injury. The almost synchronous appearance of the lesions eighteen hours after injury in all four organs suggests a single causative factor. The delay in appearance of the morphologic evidence of injury in many instances until shock has been relieved is not incompatible with a causal relationship. Days and even weeks may intervene between injury and reaction with such widely varying agents as diphtheria toxin and x-rays.

Of equal importance in establishing an etiological relationship between shock and the lesions which have been described is evidence of reversibility, of return to, or at least toward, normal with increasing intervals after the episode of shock. As all the necropsy material in this series necessarily was derived from individuals with lethal disorders, it is not surprising that a complete return to normal was not usually demonstrable. Clear evidence of a tendency to reversibility is shown in Table XVIII, in which the more severe grades of changes in the eighteen to ninety-six hour group are compared with those in the group surviving four days or longer. It is noteworthy that the time interval before recovery is demonstrable is essentially the same in all four organs, the change becoming demonstrable on the fourth day in each instance.

TABLE XVIII. INCIDENCE OF SEVERE FATTY CHANGES IN SHOCK CASES (PERCENTAGE OF CASES STUDIED IN EACH CATEGORY)

TYPE OF CASE	HEART (PERCENTAGE OF CASES)	LIVER (PERCENTAGE OF CASES)	KIDNEY (PERCENTAGE OF CASES)	ADRENAL (PERCENTAGE OF CASES)
Shock (18 to 96 hours' survival)	50	59	81	61
Shock (survival of 4 days or longer)	12	29	39	38

The possible contention that the changes described are merely agonal, like depletion of liver glycogen, is refuted by this evidence of reversibility in a large number of patients progressing to a fatal outcome due to other factors.

Though it has been repeatedly stressed that none of the changes described can be considered pathognomonic of shock, it is not impossible that the pattern of changes may be. This is suggested by Table XIX. The percentage incidence of the lesions under consideration has been compared in shock patients surviving from eighteen to ninety-six hours with three groups of control cases: a miscellaneous group of "medical" deaths, a group of aplastic anemia fatalities, and one of starvation deaths.

TABLE XIX. DISTRIBUTION OF LESIONS IN CONTROL GROUPS
(PERCENTAGE OF CASES STUDIED IN EACH CATEGORY)

TYPE OF CASE	HEART (PERCENTAGE OF CASES)	LIVER (PERCENTAGE OF CASES)	KIDNEY (PERCENTAGE OF CASES)	ADRENAL (PERCENTAGE OF CASES)
Shock cases (18 to 96 hours' survival)	75	87	76	92
Control cases:				
Starvation deaths	0	0	50	100
Deaths from aplastic anemia	33	20	25	91
"Medical" deaths	27	40	43	79

Only in the shock group do more than three-quarters of the patients show involvement of all four organs.

Subsequent to making the observations upon the adrenal gland which we have recorded, our attention was called to the investigations of Popjak[13] on the lipids in the rat adrenal in experimental shock. He found swelling of the cortex and marked depletion of both stainable and doubly refractile lipid. This occurred regularly fifteen to twenty-four hours after the shock-producing crushing injury, a time interval essentially the same as in our human material. In his animals, restitution to normal in forty-eight hours was the rule.

We have little evidence of what the significance of these lesions may be from the functional point of view. The renal lesion is discussed in our preceding paper.[14] No electrocardiograms were taken, and no determinations of adrenal cortical hormone excretion were made. The results of bromsulfalein tests in shock patients have been discussed in the first paper of this series.[15] A transitory period of retention of the dye was observed, which it seems reasonable to correlate with the fatty changes in the liver which have been described. Although no morphologic evidence of bile stasis was observed in the liver sections, the possibility of a hepatic as well as a hemolytic factor must be borne in mind in interpreting the elevated plasma bilirubin often noted in these patients.

SUMMARY AND CONCLUSIONS

Two morphologic phenomena which have been implicated in the pathogenesis of shock, pulmonary edema and pulmonary fat embolism, were studied in a series of fatal battle casualties. Pulmonary edema was found to be too inconstant and too late in development to be an important factor in the initia-

tion of shock in severely wounded men. Pulmonary fat embolism proved to be a frequent coincidental lesion. It was absent or minimal in degree in the majority of patients, and its significance in the small remaining proportion could not be established.

A standard pattern of visceral changes was found in patients with traumatic shock who survived a minimum of eighteen hours after injury. This consisted of fat vacuolation of the heart, the central cells of the liver lobules, and the ascending limbs of Henle's loops in the kidney. In the adrenal gland the doubly refractile lipid became depleted after the same time interval. In all four organs these changes persisted for three days after injury. From the fourth day onward in cases uncomplicated by infection, a tendency to return to normal could be demonstrated. The incidence of this pattern of changes proved significantly higher in shock cases than in a variety of control material. It was concluded that they constitute evidence of parenchymatous injury produced by shock.

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